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Section of Comparative Medicine

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[*October* 15, 1952]

Sites of Production of Antibodies [*Abridged*]

PRESIDENT'S ADDRESS

By C. L. OAKLEY, B.Sc., M.D., B.S., M.R.C.S., L.R.C.P.

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EXPERIMENTAL pathologists, being what they are, have brought to the problem of determining the sites of antibody production the techniques to which they are accustomed: surgical removal of organs or tissues suspected of making antibody: depression or exaltation of the functions of such suspected structures: determination of the organs in which, in a stimulated animal, antibody appears earliest or in highest concentration: transference of suspected structures into tissue culture as explants, or, as transplants, into other animals. We may consider these in turn.

Surgical excision of structures suspected of producing antibody has been attempted from the first, but the results have been so varied that little has come of it. The antigens most favoured have been sheep red cells or typhoid bacilli killed by heat: this preference for antigens whose antibodies can readily be estimated *in vitro* by simple techniques of high sensitivity but no great accuracy has persisted to the present day. Little interest appears to have been taken in the great variation in antibody response between animals injected with the same amounts of the same antigen, and it is very difficult to decide whether the variations in antibody production after surgical excisions are significant or not. Excision of the spleen, for example, has been followed by increase in antibody production, by decrease, or by results not differing from those in the controls. More recently the view has been put forward that splenectomized animals produce less antibody than normal animals do, particularly when the immunizing dose is small. If, for instance, an antigen consisting of large particles is injected intravenously in small amounts, most of it will be removed by the spleen; subsequent splenectomy removes a great deal of the antigen as well. If the antigen is injected in large amounts, some will escape the spleen and spill over into other antibody-producing tissue; splenectomy will remove only part of the antigen. In the first case, splenectomy will have considerable effect on antibody production; in the second much less. Other forms of surgical excision, such as exsanguination-transfusion, removal of the skin and the abdominal viscera seem to have little effect on antibody production.

This failure of surgical excision seriously to affect antibody production led many to suppose that antibodies were produced by tissues so diffused over the body that complete excision was not practicable. The choice of the reticulo-endothelial system for this role had a good deal to recommend it, as it was well known that many substances including antigens could be concentrated in its cells; the cells could also phagocytose bacteria; so it was natural to suppose that cells that had such intimate contact with bacteria would also make antibodies to them.

The extensive literature on this topic is almost all on depression of function by reticulo-endothelial blockade. The earlier experimenters supposed that if an animal was injected with large amounts of non-antigenic particulate material such as carbon black, and the animal was then injected with an antigen, the reticulo-endothelial cells would be so pre-occupied with phagocytosis of carbon black that they would be unable to produce antibody, at any rate in amounts comparable with those produced in controls. In fact the results have been very diverse; in some instances reticulo-endothelial blockade reduced antibody production, in others it increased it; more often it had no effect at all. It then became clear that when they were faced with large amounts of phagocytable material, reticulo-endothelial cells increased greatly in number; if they did produce antibody, then their disproportionate increase in these circumstances might increase antibody production. Only by injecting the blocking agent in enormous amounts could reduction in antibody production be made more likely. This unsatisfactory conclusion still stands, though it has recently been suggested that reticulo-endothelial cells alter antigens in such a way that other cells can produce antibody to them.

A similar interest in diffused organs had led some to ascribe antibody production to lymphoid tissue. This tissue is readily destroyed by doses of X-rays that will not damage reticulo-endothelial tissues, and can to some extent be stimulated by subjecting the animal to dry heat. Exposure of the animal to appropriate doses of X-radiation for some time before injection of antigen appears to reduce antibody production; if the spleen is shielded from the radiation much less effect is produced. Once the antibody response has started, X-ray treatment (like surgical excision) seems to have little effect on it. Stimulation of lymphoid tissue by subjecting the animal to dry heat seems to increase antibody production.

Determining the organs or tissues in which antibody appears first or in highest concentration has given far more reliable information. The earliest experiments, those of McMaster and Hudack, showed that if killed typhoid bacilli or sheep red cells are injected into the ears of mice, antibody can be detected in the lymph glands draining the injected ear earlier and in higher concentration then it can be detected in the spleen; and that this occurs whether the ears are cut off a few hours later or not. Injections into the mouse's ear, which is rich in lymphatics, pass readily through the lymphatics to the draining lymph gland. Glands draining ears injected with non-antigenic irritant material, though they develop inflammatory reactions and serum leakage comparable with those in the lymph glands on the side injected with antigen, show no comparable concentration of antibody.

The work of Ehrich's school had also shown that when the usual antigens were injected into rabbits' feet, the efferent lymph from the popliteal gland contained far more antibody than the afferent lymph. This antibody was said to be associated with the lymphocytes in the efferent lymph whose number was much increased by injection of antigen. Histocytes and polymorphs did not produce antibody but converted antigen into haptenes, which stimulated lymphocytes to produce antibody. Criticism that lymphocytes might have absorbed antibody from the surrounding lymph was countered by the observation that lymphocytes did not absorb antibody from antibody-containing fluids, and that the antibody in cells from mushes of popliteal lymph gland draining a foot injected with killed typhoid bacilli was specific. Thus if one foot was injected with *Salm. typhi* and the other with *Brucella abortus*, cells (apparently immature plasma cells) from the popliteal gland draining the foot injected with *Salm. typhi* would agglutinate *Salm. typhi* at their surfaces, but not *Brucella abortus*; while cells from the opposite gland had the converse property.

Later experiments have shown that antibody can be produced in lymph glands after injection of alum toxoids into the feet. The mere presence of high concentrations of antibody in the draining lymph gland is not the proof of local production that it is often supposed to be, for it ignores the likelihood of the leakage of circulating antibody into the inflamed lymph gland, and it involves the assumption that our methods of extraction are uniformly efficient, though it would seem evident that cellular organs like the spleen would more readily yield up their antibody than structures like skin or bone. The difficulties can be got over by

injecting two antigens, one in one site and one in another, and determining the concentration of antibody in the relevant tissue extracts: not the concentration of one antibody, but that of both. If the antibody in the tissues is due to leakage from the circulation, the antitoxin ratio of the two antibodies will be the same as the ratio in the serum: divergences from this ratio will suggest local production or storage of antibody. Moreover, however bad our methods of extracting antibody are, they will presumably be equally bad for all antibodies in a tissue, so that our extracts may be considered to yield the same antitoxin ratios as the tissue they came from. By this means it is easy to show that injection of alum-precipitated tetanus or diphtheria toxoid into the feet of horses leads to concentrations of specific antibody in the draining lymph gland far greater than can be accounted for by leakage from the circulation. As no evidence can be obtained, from horses, of any antibody production in skin, it seems reasonable to assume that the excess antibody in lymph gland is produced, and not stored, there. In rabbits, experiments show a very different arrangement. Antibody concentrations in draining lymph glands are readily shown not to be due to leakage, but it is easy to show that a similar excess of specific antibody concentration occurs in the injected skin. Moreover injection of two antigens into other structures provides evidence that antibody may be produced in rabbits in fat, muscle and cornea but not in liver, spleen or bone-marrow. No claim can be made that the antibody locally produced is formed by the cells of the injected tissue—in fact it seems much more likely that it is produced by cells entering those tissues from without.

Local production of antibody in rabbit skin makes it possible to follow the history of this process. If a primarily stimulated rabbit is secondarily stimulated with diphtheria and tetanus alum-precipitated toxoid for several days running by injecting each antigen in a separate skin square on each day, after $n + 1$ days we shall have $2n$ pieces skin, n injected with tetanus and n with diphtheria A.P.T., varying in age after injection from 1 to n days. Extraction of the pieces and estimation of concentrations of both antibodies give an antitoxin ratio for each. If the logarithms of the antitoxin ratios are plotted against time, the graph obtained is highly characteristic. For two days the antitoxin ratio does not differ from that in the serum: on the third day it begins to diverge in the direction suggesting antibody production and continues to diverge in almost a straight line, till the tenth day, after which it shows a slow fall towards the serum-antitoxin ratio. The resemblance to the graph of circulating antibody during the secondary response is very striking, and it may very well be that the circulating antibody is a mere reflexion of the activity of antibody-producing areas. For if from the third to the tenth day the antitoxin ratio in the skin follows a logarithmic straight line, surely this means that there is a logarithmic increase in antibody in the skin over that period: is it not reasonable to conclude that antibody-producing mechanisms are being developed logarithmically?

It is well known from work with isotopes that, during the fall in antibody production after the peak response to an antigen, antibody is being synthesized as well as destroyed. Glenny has confirmed this by showing that immunized horses, though they fall in antitoxin concentration when injections of antigen are stopped, do not fall to nothing: they fall to a steady level, which is higher and is reached more rapidly the more efficiently and the longer the horse has been immunized. Similar results may be obtained from antitoxin ratio experiments, from which it has been shown that horses injected in the feet with alum-precipitated toxoids, may continue to produce antibody in the draining lymph glands for at least three years.

The use of tissue culture yielded very little information on antibody production, except that antibody production did not occur in tissue culture unless the tissue had been stimulated before explantation, until the experiments of Fagraeus showed that in animals injected intravenously with killed bacilli, most of the organisms in the spleen were segregated in the red pulp, not in the follicles: and that antibody in explants of red pulp from such animals increased in tissue culture, whereas that in explants of follicles did not. Phagocytosis of organisms in the pulp was associated with transformation of reticular cells into plasma cells, and the increase in antibody seemed to be roughly proportional to the number of immature plasma cells in the explant.

Transplantation of structures likely to produce antibody has been little practised, for if the material transplanted contains no injected antigen, it will have no antigen to influence it, and if it is the injected area, the antigen may affect the recipient animal. Topley indeed showed that rabbits receiving splenic transplants from other rabbits injected intravenously with killed bacilli developed specific antibody more rapidly than they would have done if the response were on the part of their own tissues, and suggested that the transplant continued to produce antibody in the recipient animal.

Similar but more detailed information has been obtained from transplants of fat and cornea secondarily stimulated with alum-precipitated toxoids. This evidence suggests strongly that the history of a transplant, at least up to ten days after injection, is unaffected by its position, whether in donor or recipient rabbit; in either it produces antibody in much the same way. Thus, a piece of fat secondarily stimulated with diphtheria A.P.T. may be transplanted into a rabbit without experience of this antigen, and the concentration of diphtheria antitoxin followed in the recipient's serum. It is found that the shape of the antitoxin curve in the recipient depends on the age of the transplant, i.e. on the interval between secondary stimulation and transplantation. If this period is three days, the serum antitoxin of the recipient begins to rise immediately, and reaches a maximum on or about the seventh day after transplantation and then falls rapidly. This response is neither primary nor secondary: it seems to be a secondary response occurring three days earlier than normal; the first three days of the response have taken place in the donor. The use of ten-day transplants confirms this, for in these the maximum serum antitoxin concentration occurs in the recipient within about twenty-four hours, at that point in the whole life of the transplant at which the highest serum antibody concentration would be expected. By the use of two different antigens, three- and ten-day transplants can be carried out in the same animal; the peaks of antibody concentration occur independently at the expected points. If the transplant is 0 days old, i.e. if it is transplanted immediately after injection, no immediate antitoxin response occurs; this suggests that the piece of injected fat cannot produce antibody unless some change occurs in it while it is still in the donor; and it is natural to suppose that this change is due to infiltration of antibody-producing cells into it. In addition, it may be deduced from the behaviour of transplants that antibody production in an injected area is far more efficient than it is in the rest of the animal—probably at least 800 times more efficient weight for weight.

This has an important bearing on a recent view of the nature of the secondary response to an antigen. This suggests that when an animal is primarily stimulated, antibody is stored in the tissues; secondary stimulation acts as a non-specific stress, as a result of which ACTH is secreted by the pituitary; this stimulates the adrenal to secrete a hormone that causes the antibody-filled tissues to empty their antibody into the circulation. If this hypothesis were true, one would expect that any noxious stimulus would give rise to a non-specific secondary response and that this response would be uniform all over the animal. In fact little stored antibody can be detected in the tissues of animals long after a primary stimulus; and local injection of an antigen as a secondary stimulus gives rise to a specific response which is far more efficient locally than it is elsewhere; this local response may continue for years. It seems much more probable that the antibody thus released is being built anew than that an unidentifiable precursor is being converted into antitoxin, especially as the conversion would have to be more efficient in the injected area.

We may conclude, then, that in horses antitoxic antibody is produced in draining lymph glands; in rabbits it is produced in skin, fat, muscle and cornea, and in draining lymph-glands, though not necessarily by the special cells of these structures; and that production is much more efficient in injected structures that are capable of producing antibody than it is elsewhere in the animal.

Section of the History of Medicine

President—
The Right Hon. Lord WEBB-JOHNSON, K.C.V.O., C.B.E., D.S.O., T.D., M.B., F.R.C.S., LL.D.

[*October* 1, 1952]

The Water Doctors of Malvern, with Special Reference to the Years 1842 to 1872

By W. H. MCMENEMEY, M.D.

THE beautiful range of hills to the west of the Vale of Evesham and the Severn Valley has from early times been noted for the curative value of the spring waters. Richard Bannister in his *Breviary of the Eyes* (1622) writes:

> "A little more I'll of their curing tell
> How they help sore eyes with a new-found well
> Great speech of Malvern Hills was lately reported
> Unto which spring people in troops resorted."

John Wall.—The six sleepy hamlets snugly tucked in hillside pockets grew with the years and housed the sick in search of the health-giving waters, but no attempt was made to develop Malvern as a spa until John Wall, a one-time Fellow of Merton College and one of the original physicians of the Worcester Infirmary, told of remarkable cures which he had observed there. Was it to be wondered at, for had not Hippocrates, Horace and Tasso all observed that mountain springs which faced the rising sun had healing properties? Wall described patients with scrofula, sordid ulcers, fistulas and palsies who had toiled up the hillside to refresh their withered limbs in the spring waters. One lady, it will be recalled, so far recovered from her blindness as to be able to discern the fleas hopping on her bed.

Wall's monograph, first published in 1756 with a view to raising funds to provide proper accommodation at the wellside, went through two subsequent editions and the popularity of Malvern grew to such an extent that public breakfasts, assembly balls and an annual venison feast were held. The aristocracy patronized the spa and sharpened their jaded appetites in the mountain air, while their fashionable ladies graced the terraced walks adjoining the hotels and John Dugard's commodious lodging house where for fifteen shillings a week one was provided with full board, including tea, coffee, fire and candles. Benjamin Stillingfleet, the botanist, writing in 1757 to Mrs. Elizabeth Montague, speaks of the wonderful waters but adds: "I do not doubt but that the air and exercise, which at present is absolutely necessary here, the well being about two miles from the town, contribute very much towards restoring the health of the patients." Wall carried out an analysis of the spring waters with the aid of William Davis, the Worcester apothecary, commenting on its extreme purity; hence it was echoed:

> "The Malvern water, says Dr. Wall
> Is famed for containing just nothing at all."

Wall retired to Bath in 1774 and died two years later. Thereafter the popularity of Malvern as a health resort waned.

John Wall's younger son, Martin, Clinical Professor of Medicine at Oxford, had samples of the water sent to him for analysis and, in a reprinted edition of his father's work published in 1780, was able to substantiate his findings. Evidently patients still made use of the waters, for Thomas Warton in his *Ode on His Majesty's Birth Day*, wrote in 1790:

> 'Health opes the healing power her chosen fount
> In the rich veins of Malvern's ample mount."

A. Philip Wilson, an Edinburgh graduate and a physician of Worcester, who later changed his name to Wilson Philip, made good use of the Malvern waters and published his analysis in the year 1805. In 1831 William Addison, a practitioner of Malvern and a clinical microscopist who published much in the early days of the Provincial Medical and Surgical Association, wrote in a volume dedicated to the Duchess of Kent, whose physician he was, that Malvern was "annually becoming more and more the resort of visitors and invalids seeking health or protection from disease". The Hereford Mail left the White Horse Cellar, Piccadilly, at 8.30 a.m. and reached Malvern village at 3 p.m. the following afternoon.

James Wilson and James Manby Gully.—But the prosperity of Malvern really began with the advent of James Wilson and James Manby Gully in 1842. Wilson, then aged 35, had spent his early years in North Wales and had been educated in Dublin, London and Paris, where he had studied with Broussels. For some time he was resident surgeon in the Liverpool South Dispensary and then he bought a practice in Sackville Street, off Piccadilly, but sold it in 1840 in order to accompany Lord Farnham on the grand tour. Finding this old gentleman too exacting, however, he parted company and before long found his way to Graefenberg, where he came under the spell of Vincent Priessnitz, both as a patient and a pupil.

Gully, born in Kingston, Jamaica, the son of a coffee planter, was a year junior to Wilson and was educated in Liverpool, Paris (where he was a pupil of Dupuytren) and Edinburgh. Under the Emancipation Act of 1832 he was deprived of all prospects of his father's great wealth, so that in order to supplement the precarious livelihood of a young physician, he had recourse to translating and writing.

A fondness for music had brought these two physicians together but they had other things in common: they had each studied in Liverpool and Paris, and they had a distrust of orthodox medicine. I suspect that the experiences of James Currie of the Liverpool Infirmary, who had so successfully treated fevers and other diseases with hot and cold water, were fresh in the minds of both of them. Currie, it will be recalled, had developed this form of therapy after hearing William Wright relate how, when stricken with fever *en route* from Liverpool to Montego Bay, he had ordered the deck hands to throw buckets of sea-water at him, with speedy and complete success. Wilson, too, had studied with James McCartney of Trinity College, Dublin, who made use of water dressings in sickness. "If men knew the properties of water", McCartney had said, "and how to apply them so as to produce all their effects, water would be worth more than all other remedies together." Five years before coming under the spell of Priessnitz and while still in Sackville Street, Wilson had written a monograph on the curative effects of simple and medicated vapours applied locally.

At Graefenberg the keen mind of Wilson soon saw the medical possibilities in the ideas of Priessnitz, the modest and illiterate peasant, who had so quickly achieved an international reputation as a healer. Priessnitz had not forgotten his early struggles against orthodox medical practitioners, who had resented his intrusion into the realm of therapeutics, but had taken comfort when the judge, having asked a patient which of the two, the plaintiff doctor or Priessnitz the defendant, had cured him, was told: "Why both, your honour, the doctor relieved me of my money which went for the drink and Priessnitz of my gout." Nevertheless, Priessnitz had many medical pupils, but he eyed them all with suspicion. "Doctors have learned too much", he would say, "they have neither knowledge nor faith in the healing virtues of cold water and therefore do not use it with the necessary confidence."

Disease was due to vicious humours, the result of drugs and too much food. It was his aim to expel the bad juices. To this end he made his patients exercise until they were ravenous. Potatoes he allowed only in winter because, he maintained, they interrupted digestion and sleep. Hunger, the autocrat, we read, reigned supreme at Graefenberg.

Wilson was a diligent and observant pupil and on his return to England sought out his friend Gully; they decided that the Worcestershire highlands most nearly represented the climate and landscape around Freiwaldau in Silesia. One morning in the month of May 1842 Wilson and Gully surveyed the city of Worcester with some curiosity, wondering if the roar of the local medical lions, and in particular Charles Hastings, would be heard eight miles away in Malvern, and joined the Hereford coach at the Star and Garter. An hour later they pulled up in front of the Crown Hotel. A few stragglers, who welcomed this daily excitement of the arrival of the Royal Mail, and the postman in his smock—for he was also the milkman—were the only ones to witness the coming of the doctors who were so quickly to transform this village into a prosperous town.

Wilson settled in the Crown Hotel, bought the lease and before long it was known as Graefenberg House. Gully returned to London to wind up his affairs before joining his partner in Malvern. Wilson's first patient was the local carrier, aged 64, a notorious drunkard who suffered from the gout and complained of stomach pains and cramps in his legs. Wilson, who found his patient thin, haggard, subicteric and asthmatical, had him well in ten days, attributing his disorder most provocatively to the arsenical treatment which Hastings had prescribed. It is not to be wondered at that this unfortunate patient became a *causus belli* between Hastings and Wilson. The temporary improvement in the health of the carrier was the means of inducing the local plumber and glazier to consult the water doctor and also a 75-year-old man who, crippled with rheumatism to such an extent that he had his chin bent down to the breast bone, must have presented a problem in rehabilitation to the enterprising Wilson. Thereafter, patients flocked to him and soon the little village was early astir with bath attendants passing from house to house at 5 o'clock in the morning. Wilson wrote two books in quick succession, styling himself Physician to His Serene Highness Prince Nassau: the second volume on "stomach complaints and drug diseases" was dedicated to "the suffering and much-abused stomachs of Her Majesty's faithful subjects" and it included an engraving of Napoleon at St. Helena in his second year of his cancer of the stomach. The causes of stomach disorders, said Wilson, are food, physic and fretting. Water was the sovereign remedy for everything. The body was largely composed of water, wrote one hydropathist, so one used water to repair the body just as one used cloth to mend a jacket or glass to replace a broken window.

Wilson and Gully were not the first to practise the hydrotherapy of Priessnitz in this country. Richard Claridge, a captain in the Middlesex Militia, who was at Graefenberg with Wilson, published an enthusiastic account of the water treatment in January 1842 and founded societies for encouraging the cult. A Dr. T. J. Graham had, however, already opened a hydropathic establishment at Stansteadbury, Hertfordshire, late in the year 1841, the medical director being Joseph Weiss, formerly of Freiwaldau, while C. von Schlemmer had set up as a water doctor at Ham, Surrey, in December 1841, moving to Stansteadbury in the following June. Neither Stansteadbury nor Ham achieved the fame of Malvern, whither patients came from all over the world.

Wilson and Gully soon parted company and an estrangement ensued, which happily was remedied in later years. The Crown Hotel, which Wilson took over as Graefenberg House, is now, according to my friend Mr. Howard Mitchell, replaced by Lloyds Bank; it lay between the Mount Pleasant Hotel, which still flourishes today, and the former Bellevue Hotel, now shops. Wilson later, at a cost of £18,000, built Priessnitz House which eventually became and remained, until a few months ago, the County Hotel. Gully built two embattlemented buildings, Tudor House for men and Holyrood House for women; they were joined by what the men patients called the Bridge of Sighs. Together they now constitute the Tudor Hotel, on the main road to the Wells, just a couple of hundred yards beyond Bellevue Terrace.

The bath.—The general plan was the same wherever you went. You were called at 5 a.m., stripped by your bath attendant and wrapped tightly in a cold wet sheet and packed in blankets. At first you shivered but gradually a warm refreshing glow developed and you sank into blissful slumber. An hour or so later the attendant returned, you were released from your envelope and requested to sit in a portable bath while a pitcher of coldish water was poured over you. After dressing you met your fellow patients and set off up the hillside with your Graefenberg flask in your pocket and instructions to drink at the springs. Wilson himself on one occasion at Graefenberg consumed thirty flasks before breakfast. He claimed it made one cheerful, hungry and wide awake. "You wash your face with water", he said with some conviction, "so why not your stomach, too." Bulwer Lytton (who later became Lord Lytton) once wrote:

"Amongst all my most brilliant recollections I can recall no periods of enjoyment at once more hilarious and serene than the hours spent on the lovely hills of Malvern. . . . The rise from a sleep as sound as childhood's—the impatient rush into the open air while the sun was fresh and the birds first sang—the sense of an unwonted strength in every limb and nerve—the delicious sparkle of that morning draught—the breeze that once would have been so keen and biting, now but exhilarating the blood and lifting the spirits into religious joy."

Charles Dickens, however, a patient of Gully's, tells of "cold-waterers" dashing down the hills with severe expressions on their countenances "like men doing matches and not exactly winning". Another speaks of the chilled appearances of the patients at the wellside, as if they were in need of blood rather than water.

Breakfast served at long tables in a large dining-room consisted of bread and butter, treacle, milk and, if you still wanted it, water. After breakfast you saw the doctor and received your bath orders for the day. The rest of the morning was free unless you had been condemned to the cold douche, when you awaited your turn in the garden or played battledore and shuttlecock in the recreation room. A healthy patient who was making good progress, as indeed most of them did, was deemed fit for the douche about the tenth day. The douche baths were at the end of the lawn in a series of wooden houses, and the ordeal amounted to a hogshead of cold water discharged in a torrent lasting from a half to one and a half minutes through a pipe three inches in diameter from a height of twenty feet. One victim who had descended the steps into the execution well wrote: "When it struck me straight

on the shoulder it knocked me clean over like a ninepin. . . . A momentary rush, like a thunderstorm, was heard over me, and the next second the water came roaring through the pipe like a lion upon its prey and struck me on the shoulders with a merciless bang, spinning me about like a teetotum." Not all the stories retailed by the bath attendants were calculated to assuage the anxieties of the awaiting victims. One man had been hit by a heavy icicle which caused his back to bleed. An old lady, with a view to shortening the fall of the stream, stood on a chair; but the added weight of the torrent caused the chair and the patient to collapse in confusion. Neither age nor sex excused a patient. The anonymous author of "Three Weeks in Wet Sheets" said that most of the promenaders were called away in turn. A door would open and a bath woman would make a cabalistic sign to one of the young patients, who would obediently disappear into the appointed hut. A minute or two later one would hear her half-frightened half-ecstatic shriek of nervous delight as the torrent fell on her fair frame.

The regimen.—Dinner at Priessnitz House was served at 3 o'clock, the doctor sitting at one end of the table and Mrs. Wilson at the other. The doctor carved the boiled mutton—and it was always boiled mutton—and his wife dispensed fish. The occasion, wrote Richard Lane, called for a white neckcloth.

One visitor was impressed by the appeal of the cult to young ladies: "Six bright-eyed houris, whom you would sooner expect to meet in Mahomet's heaven than in a hydropathic hospital, sat opposite to us. . . . They set to like so many giants refreshing themselves. No dainty woodpeckers were the young ladies . . . they worked with knife and fork like Amazons, while looking as delicate as lilies of the valley." Amongst his companions at table he caught the guilty eye of a man whom he had seen in the Bellevue Hotel on the previous evening furtively order and hastily dispatch a brandy and soda. Strict temperance was the rule and it was woe to those who were caught with contraband food on their persons for Wilson spurned the delicacies of the confectioner and abhorred strong waters and pickles and spices. One writer describes how he had to repair to a churchyard in order to devour an illicit basketful of rich Mogul plums. Another had to cross on to the Herefordshire side of the hills in order to enjoy a cigar.

In the afternoon one relaxed—perhaps a coach drive to view the conservatories at Madresfield Court or the beauties of Eastnor Castle. Then came the sitz bath which, according to Edwin Paxton Hood, did more than anything else to foster an ultra-democratic atmosphere, for in the hydropathic establishments noble lords, honourable gentlemen, baronets, captains, tradesmen, ladies of rank and ladies who wished to be thought of rank, were all to be seen together, even sitting on the same sofa. There was a total freedom from caste. It was quite extraordinary and showed the adaptability of the English temperament. Plebeian and aristocratic blood were alike subject to the ills of mortality and to the indignity of the sitz bath. Everyone knew that everybody else was daily submitting to it. It was most humiliating. Its purpose was sedative and it was explained to patients that the whole of the intestines lying in the vicinity of some of the most important secretory organs would be enabled by the action of the water to throw off in fifteen or twenty minutes a large proportion of caloric. It helped to cool tempers and it was a "mighty tonic". Gully recommended it particularly to the tired business man before settling down to his evening meal, especially if a cold wet cloth were at the same time applied to the head. It was described as a woman's best friend.

Supper, consisting of bread, butter, biscuits, milk and a final round of water, followed at 8 o'clock and after some songs and parlour games everyone went to bed early to prepare for the ordeals of the next day. In the heyday of the cult a band played at Priessnitz House and there was dancing.

The cost.—The charges at Graefenberg House were four guineas a week to include full board, baths and medical attention, with an initial consultation fee of one guinea, later raised to two. You had to provide yourself with one blanket and two coarse sheets. Hastings taxed Wilson with making the treatment expensive, but he denied the charge. Rumours were not always correct, wrote Wilson to Hastings: It was for instance currently reported in London that he, Hastings, had placed himself under Wilson's care and that as a result his health had been perfectly restored. Wilson accused Hastings of having examined a young patient of his while he was supposed to be treating her father. The correspondence between the doctors was bitter and unforgiving.

Wilson was described as an impressive man with silky curled whiskers, quick, full of impulse and of the fire of genius; he was kind but exacting. He spoke seven languages and had an imposing array of books in his library, including seven hundred volumes on the subject of water. He was often to be seen on a thoroughbred bay mare in the village or on the hillside rounding up his patients like so many sheep. He would consult with many on the way up to the Wyche cutting and ask to see their tongues. Gully said of him: "I never knew one with a quicker eye for disease. No man was better abused by the ordinary medical press and medical crowds than Wilson, but there was more acuteness in his little finger than in the brains of those who barked at him."

Gully, by contrast, was dignified, staid but pragmatical: he was short of stature and inclined to be stout: he stood characteristically with arms akimbo. When he rode through the village he was followed by a liveried servant. He has been described as a genius with a master mind; he was profound, penetrating and resourceful. He seldom failed to fascinate a patient. His ruddy face, mostly lighted with a smile, seems to have satisfied Gladstone, Macaulay, Dickens, Charles Reade, Carlyle, Tennyson,

Darwin, Bishop Wilberforce and Florence Nightingale, to mention a few of his patients. He must have possessed considerable personal magnetism.

Spencer Wells was his patient in the late spring of 1851 for a stay of six weeks and his visit must have surprised and annoyed Hastings and his colleagues in Worcester: he had but recently recovered from pneumonia and lung expansion was deficient. Gully told him to eat only bread and lean meat, to live in the open air and take the water treatment.

Type of patient.—For the most the water doctors were consulted by patients suffering from overwork, overindulgence, lack of exercise, insomnia, and nervous dyspepsia, but they seem to have treated gout successfully. Valetudinarians comprised a large part of their clientele for there came toMalvern, we read, those who "had eaten whole cabbage gardens and turnip crops in vain attempts to get well". But Gully, more than his colleagues, seems to have gone in for genuine bed-patients. In fact as a water-curer he was second only to Priessnitz in reputation.

The water doctors reigned supreme over their patients. One observer says: "The Marquis of Anglesey, hero of Waterloo, who could chop up ironclad cuirassiers like so many lobsters in their shells, was as deferential to the Water Doctor as a drummer boy . . . Barristers who bullied the Queen's Bench cringed to the Water Doctor, while bluff Admiral "Go-it-Ned" Codrington, who blew Turks about like sparrows, followed the hydropathic leech with the fawning docility of a poodle . . . he was as jolly as a sandboy amid broadsides but he struck his colour before the first discharge of the Douche."

There was no respite even for those who at a reduced fee of three guineas boarded out. Visitors in one inn noticed an old man fresh from the summit of the Worcestershire Beacon consume with relish a plateful of bran and oatmeal mixed with two round vegetables which were either potatoes or yams. They had heard of the black broth of Sparta but had never seen human beings eat bran. But they stared with wonder and concern when they saw him embellish his antiphlogistic meal with a whole bottleful of plain cold water.

Another form of hydrotherapy was the lamp bath introduced by Gully. The patient sat swathed in blankets; under the chair was a lamp which gradually provoked the desired effect and as the sweat poured off the patient the attendant would hand him a glass of cold water "to prevent him from boiling over". When asked if anyone had actually been burnt under treatment, the attendant once replied coolly: "I have known of two instances" and with supreme tact added: "but they occurred at another establishment." Paxton Hood says: "There is nothing so likely to draw the gravy out of a man as the lamp bath." He describes seeing a London alderman, in whose bowels, as he put it, lay entombed creatures of the heavens, the earth, the air and the sea. "Never", he wrote, "did the big drops stand out on the brow of guilty malefactor more heavily than on the face and forehead of our poor suffering alderman . . . his head rising up in all its baldy ruddy Olympian grandeur out of a mighty pyramid of towels . . . that is the process for taking the black blood out of a man, that is the way to purify his skin, and rouse and energise his liver." You could, it was rumoured, recognize an alderman in the lamp bath by the smell of turtle fat! He explains the rationale of the treatment. The allopath would have made use of the lancet for in the overindulged patients the blood is carbonized, black or dark-coloured. The allopath takes it away from you altogether but the hydropath strains it through the skin.

The Neptune girdle.—Then there was the "Neptune girdle" or the Umschlag which Priessnitz practised on himself with such success when, as a youth, he was run over by a farm cart fracturing his ribs. It was simply a cold wet compress worn around the abdomen and protected by an india-rubber covering: it was removed before meals and then a new one applied afterwards. Nearly everyone wore it. The theory of it was that it increased the heat of the stomach and therefore assisted digestion. "However gorgeous the old dowager is dressed at night", wrote one of Wilson's patients, "she's in reality underneath as moist as a frog, and the curry-eating old Indian is hissing like an urn-iron in a full suit of wet swaddling clothes."

Wilson and Gully succeeded then in reproducing faithfully at Malvern the atmosphere of Graefenberg. Freiwaldau became Malvern Link and Graefenberg Great Malvern; the Marien, the Joseph and the Ferdinand springs were represented by the Holywell, the Haywell and the Chalybeate springs; the Springs of Friendship and Good Hope by St. Anne's Well; the Bernstein by the Wyche cutting; the Hamburg path by Happy Valley; Oswald's Joy by the Beacon; the Hirschbad Kamm by the Malvern and Abberley range; the Valley of the Staritz by the valley of the Severn, and the range of the Altvater by the Sugar Loaf at Abergavenny. And to be sure, the Archduke Franz Karl, the Duchess of Anhalt-Koethen and the Prince Bishop of Breslau, who patronized Priessnitz, had their opposite numbers in Malvern and many more besides. The doctors galloped on the hillside just as Priessnitz had done in Graefenberg.

The regimen was the same and the diet similar, although at Malvern more sympathy was shown to dyspeptics: but wild strawberries and cream, alas, so popular for breakfast at Graefenberg, were not available in Worcestershire. The master minds of Wilson and Gully seem to have catered carefully for the morale of the patients, for we learn that at St. Anne's Well they drank "to an andante of

Haydn's, a potpourri of Donizetti or the measured time of the Pressberg polka". This German band was invigorating the patients as early as 6 a.m. The modest premises at St. Anne's Well seem to have provided for the patients club-like facilities to compare notes on their treatment and, when the doctors were out of sight, to supplement their diet: here one could hire out knives and forks for a picnic, or eat devilled kidneys with impunity.

J. L. Marsden.—Before long another water doctor appeared in the person of James Loftus Marsden, a practitioner of Exeter, who had been converted to homœopathy after his only son had recovered from typhus complicated by "water in the brain and inflammation of its base". Marsden spent five months with Priessnitz (probably in the autumn and winter of 1845–46) and then accepted an invitation from Gully to join him in partnership for a limited period. He settled at Hardwicke House. He was a prodigious worker. One admirer described him as a man with no special originality who did honest yeoman service in the cause. He provided novelties for the patients by prescribing pulsatilla of the twelfth potency, a duodecillionth of a grain of ipecacuanha and infinitesimal quantities of china, aconite and secale cornutum. "What nonsense it all is", railed the allopaths of Worcester. But Marsden was more tolerant. Their violent language was the offspring of anger and not of philosophy. Had not analysis made it abundantly clear that the efficaciousness of the spring waters was due to the high dilution of the solids they contained?

Hydropathy had caught the eye of the public. When Edward Johnson returned from Graefenberg in March 1843, four hundred tickets were sold for his lecture at the Society of Arts, and a mass of people were unable to gain admission. In the year 1846, however, water doctors met with a crisis. Dr. James Ellis, of Sudbrook Park, was charged, on the evidence of local practitioners, with manslaughter, one of his patients having died under treatment. But the coroner absolved him from blame because the pathologists had omitted to examine the brain and so the possibility of a natural catastrophe could not be excluded. With this trial hydropathists won a moral victory over the drug doctors. Earlier in the same year Dr. (later Sir John) Forbes had written favourably of the water cure in the *Foreign and British Medical Quarterly Review*. The Worcester doctors, who had always found Malvern a profitable hunting ground for guineas, were beginning to lose their Worcester patients also.

R. B. Grindrod.—Ralph Barnes Grindrod, a temperance reformer and another disciple of Hahnemann, was a remarkable individual who set up his establishment about the year 1851 at Townsend House. It is believed that he received his licence to practise about 1830 but in the year 1855 he was one of two recipients of the doctorate in medicine of Lambeth bestowed by Archbishop John Bird Sumner.

One of his patients wrote:

"He is in truth a most lovable and delightful man. He lives for his patients and in the study of their state, their wants and their comforts, and all love him and trust him." ... A portrait of Priessnitz (the "Columbus of Health") hung in the breakfast parlour, and over the chimney-piece in the consulting-room, adorned with medical memorabilia, was an engraving, appropriately enough, of the battle of Worcester.

Grindrod was particularly skilled at rehabilitating those whose livers had been unduly taxed in India. Certainly the food was of the blandest and the psychological approach to it must have been skilfully handled, for we read that after the meat course "various puddings, tapioca, sago, bread and rice rise to the charmed eyes of the enamoured spectators". On Thursdays the learned doctor would deliver public lectures in his spacious winter garden surrounded by the fossils in his geological museum. Spencer Wells once formed a part of the fashionable gathering which, after the lecture, promenaded through the grounds admiring the flowers or amusing themselves with a game of bowls or a trial of the ninepins. If you were a particularly favoured patient Dr. Grindrod would show you the trilobites found in the new railway cuttings, or allow you to look at objects of interest through his beautiful microscope.

Dr. Grindrod was one of the first in this country to make use of the compressed air bath which had been developed by Emile Tabarié at Montpellier and subsequently published for the Institut de Paris in 1832. The idea was not new, however, for a Dr. Henshaw in 1664 had planned a "domicilium" on a speculation of Robert Boyle, in which air would be pumped in under pressure for therapeutic purposes.

In an iron chamber a dozen patients full of faith and fully clothed would sit while the pressure was slowly advanced half an atmosphere, Dr. Grindrod in the control room observing their reactions with interest through a glass window. Burdon Sanderson praised this "important remedial agent" as he called it. Many diseases could be relieved by this treatment, it was claimed, and we read a pathetic account of a youth in the very last stages of pulmonary tuberculosis being carried into the chamber so that some small relief might be vouchsafed to him.

That the sexes should have been mixed at the establishments of Wilson and Grindrod, as in Graefenberg, excited much comment in Victorian England. By means of bath attendants might not the infirmities of female patients become known to everyone with whom they sat at table? One of

Grindrod's supporters admitted that this would theoretically be possible in reference to a low and vulgar class of uneducated patient, but it was certain that no *gentleman* would for a moment tolerate the gossip of a mere bath attendant.

Other medical settlers.—Other water doctors settled in Malvern and all of them did well. Dr. Ayerst built Wells House (now a school). Dr. Paisley was at West Malvern. Edward Johnson, an early pupil of Priessnitz, who had practised at Stansteadbury and at Hockley Heath near Birmingham, eventually came to Malvern in the early fifties and practised at Malvernbury, now a nursing home, and Ellerslie, now a girls' school. He was succeeded by one of his five doctor sons, Walter, a protagonist of the art of anatripsology. Rubbing with brandy had quite a vogue in Malvern.

Dr. Leopold Stummes was an assistant of Wilson's but he moved to Grasmere and later to Torquay.

The Worcester to Hereford railway was opened in 1859: patients now flocked into Malvern and great wealth poured into the pockets of the water doctors. Gully's income exceeded £10,000 a year. Lithographed portraits of the rival doctors in shop windows and on the walls of inns seem to bid for possession of the visitor's body on arrival in the town. Numerous books on the water cure emanated from Malvern and there was even a periodical, the *Hydropathic Record*. Malvern was described as a human laundry for the washing out of disease: one rinsed out the blues, although some retained their starched appearance to the end.

But with increasing competition to secure patients the individual discipline was relaxed: tea and coffee appeared on the menus and soon the day began later, *and* with porridge, and bacon and eggs.

In the early sixties Hastings, who for some years had been living in Malvern, led a second attack in the columns of the *British Medical Journal*, this time against those who made the water cure the pretext for the practice of homœopathy. Spencer Wells took part in this correspondence on the "Malvern Water Works" and expressed his indebtedness to Gully. Referring to his own treatise on gout, published in 1853, he wrote: "a further experience of eight years fully confirms me in the opinion I there expressed as to the good effect of hydropathic treatment, combined with pure air, cheerful society and absence from all domestic troubles, cares and anxieties. What I practise I have openly professed and urged upon others: but I deny that, by recommending hydrotherapy I have in any way supported homœopathy."

He believed Grindrod was a homœopath. Grindrod denied this and attacked Gully asserting that *he* was a homœopath and that he had actually seen globulistic prescriptions in his handwriting. This further correspondence prompted the editor of the *British Medical Journal* to write "whoever innocently sends his patients to Malvern . . . is sure to have a determined democrat of a homoeopath returned upon his hands. . . . Between the Scylla of hydropathy and the Charybdis of homoeopathy the faith of any honest believer in old-fashioned medicine who visits the Malvern shrine is in great danger of being shipwrecked at the waters there—his belief in old physic clean washed out of him". The profession had only itself to blame. Instead of welcoming hydrotherapy they had snubbed the Silesian peasant and his disciples. The result was that a grand therapeutic agent had fallen into the hands of joint stock companies and clever enthusiasts. Incidentally the reaction of the profession to hydrotherapy had been accurately forecast in *The Times* of February 14, 1842.

When Dr. Gully eventually took up his pen he wrote: "In spite of all the bitterness and bigotry with which the sectarians of the medical profession denounce each other, a certain amount of catholicity of view regarding medical treatment is gradually taking possession of the non-professional mind."

Wilson died in 1867. Gully left Malvern in 1872 and died in 1883. With his departure the water cure in Malvern received a blow from which it never recovered. Gully sold his practice to Dr. Fernie who moved to London in 1887. Marsden moved to London, but Grindrod remained in Malvern until his death in 1883. Dr. Rayner, another recipient of the Lambeth Degree, who had purchased Wilson's practice, died in 1891 and there ended the Malvern water cure. Townsend House became a Benedictine monastery: it is now part of Malvern College.

The passing of hydropathy.—Why did the cult of hydropathy die? In Malvern, for four reasons I think: firstly because of the passing of three great personalities, Gully, whom I would list first in importance, Wilson and Grindrod; secondly because as a group they were not content to practise hydrotherapy alone or with orthodox medicine, but flirted with homœopathy, thereby antagonizing many well-wishers in an age of professional intolerance; thirdly because of the drying up of some of the wells; and fourthly because of improving rail facilities, so that Britons in search of health found it more satisfying to visit the German, Bohemian or French spas, where the gaming tables being legitimate provided an exciting adjunct to the cure. But another Wilson might succeed even to-day, for there are many who would be attracted for a time by the discipline of a semi-spartan existence: which of us does not envy the experience of Lord Lytton, and would not enjoy being so re-created?

These men, who in their day were regarded by the profession as quacks, did much for Malvern, more in fact than the railway; between 1842 and 1867 it grew from a village to a prosperous town. During their lifetime they helped to educate the public—and the medical profession—in the way of health: indeed, their doctrines constitute an important chapter in Victorian medicine. They would be gratified to find that the town which they built is now a health-loving community of schools.

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Section of Psychiatry

President—The Hon. W. S. MACLAY, O.B.E., M.D., F.R.C.P., D.T.M. & H., D.P.M.

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Death Due to Treatment

PRESIDENT'S ADDRESS

By The Hon. W. S. MACLAY, O.B.E., M.D., F.R.C.P., D.T.M. & H., D.P.M.

THE subject of this Address is not the result of a fit of depression nor is it an attack on physical methods of treatment. It is a plea for careful consideration in each individual case of the possible damage as well as the possible benefit that may come from treatment; considered assessment of this implies exact knowledge of possible complications, the most important being death.

I have restricted my investigations to death as a complication of treatment and have not considered the wide field of other complications about which more knowledge is needed. My reasons for doing so are three: First, I believe in the sanctity of human life and that it should not be lightly thrown away even in persons whose bodies or minds are deformed. We know of cultures and civilizations where it was customary to kill at birth twins or any child who showed a physical deformity; we know of the custom of putting old people out to die when they cease to be useful. We regard these ways of life as uncivilized but it is not very long since large numbers of mental hospital patients were sent to the gas chambers and even in this country at the present time one often hears the remark "What is the use of keeping these people alive". In my view the treatment of the mentally ill may well justify taking risks but the risks must not be lightly taken merely because the patient is mentally abnormal.

My second reason is that if death occurs as the result of a treatment which is not for purposes of urgently saving life it is a dramatic and irreversible complication which no one can disregard as being of minor importance.

The third reason is that my official position with the Board of Control enables me to hear about all the unusual deaths occurring in mental hospitals and M.D. institutions in England and Wales thereby giving an overall picture difficult to achieve in any other way. The information available is in the reports of deaths sent to the Board of Control, letters to Coroners, depositions at inquests, post-mortem reports and in some instances additional facts provided by medical superintendents.

I have been through the records for the last five and a half years (1947 to end of June 1952) in order to pick out the deaths which seem to be directly attributable to the treatment being given.

Table I shows the main causes and numbers of deaths due to treatment. The total is considerable when one thinks in terms of individuals and not of statistics and percentages.

TABLE I.—TREATMENTS WHICH CAUSED DEATHS

Leucotomy	180
Convulsion treatment (including electronarcosis)	67
Insulin	44
Anæsthetics	13
Continuous narcosis	8
Malaria treatment	6
Surgical operations	6
Intravenous injections	3
Drugs for epilepsy	2
Psychotherapy	—
Total	329

I would stress that this is not a statistical paper. My hope is that a factual survey of the numbers of deaths and their post-mortem findings will be useful and of interest to those who every day are using treatments that have caused them.

Electric Convulsion Treatment

Clearly it is impossible to discuss in detail all the subjects covered in Table I. I shall deal mostly with deaths due to E.C.T. as the numbers that occur in any single individual's experience are invariably small. One doctor stated that prior to the death he reported he had given 5,000 treatments without a fatality, yet another that in his hospital where E.C.T. was used actively there had been no mishap in three years.

An investigation of the use of shock therapy in 305 mental hospitals in the U.S.A. carried out by Kolb and Vogel in 1942 gave a death-rate of 0·06%, so there is justification for the remark by Sargant and Slater (1944) that the risk of death is usually negligible, though the operative word is the qualifying adverb "usually".

In 1944 Napier reported 6 deaths and believed them to be the only deaths that had occurred in this country. In 1948 Will, Rehfeldt and Neumann reported on 33 deaths due to E.C.T., these being all that they could find reported in the medical journals of their own and other countries.

Excluding the 5 deaths due to electronarcosis there were 62 deaths (25 men and 37 women) in my series. 4 deaths occurred in 1947, 3 in 1948, 13 in 1949, 14 in 1950, 19 in 1951 and 9 in the first half of 1952. It would appear that increased experience has led to an increase rather than a decrease in deaths. I suspect that this increase is not due to a wider use of E.C.T. but to a greater boldness in its use on patients who were previously considered too grave a risk. This may be caused by the feeling of safety induced by the use of relaxants such as curare, about which I shall have something to say later, or to an increasing appreciation of the frequency in the aged of depressive illnesses that can be benefited by E.C.T. This seems to be borne out by the age groups as shown in Table II.

Table II.—Age Groups of E.C.T. Deaths

Years	26–35	36–45	46–55	56–65	66–75	76–85	
Number of patients	6	10	11	21	9	5	Total 62

It shows that the majority of the deaths (35 out of 62) were in persons over the age of 55 years and that only 6 were under 35. Of the 6 in the youngest age group 4 were sufficiently unusual to be considered exceptional. It appears that under the age of 35 years death is very unlikely to be caused by E.C.T.

Table III shows the findings reported as the cause of death.

Table III.—Causes of Death after E.C.T. (Total 62)

Cardiovascular system			
Cardiac failure	22	34	
Coronary occlusion and atheroma	10		
Primary cardiac arrest	1		
Vagal inhibition	1		
Respiratory system			
Respiratory failure	6	19	
Lobar or broncho-pneumonia	4		
Acute pulmonary œdema	3		
Bronchial obstruction	2		
Pulmonary embolism	3		
Pulmonary collapse	1		
Cerebral			
Cerebral fat embolism	1	4	
Pontine and medullary hæmorrhage	1		
Hæmorrhage in internal capsule	1		
Pinpoint hæmorrhages in medulla	1		
Collapse under anæsthesia			1
Anoxia			1
Status epilepticus			1
Ruptured intestine and peritonitis			1
Toxic goitre			1

According to Alexander and Lowenbach (1944) there are 3 possible mechanisms for fatalities: (1) The direct action of the current on the brain tissue resulting in vasoconstriction; but to bring this about requires in animals much greater amperage, duration of flow and density of current than are used in man. (2) Excessive stimulation of the vago-vasomotor centres of the medulla causing generalized circulatory disturbances. This mechanism would only operate if the electrodes were placed in too posterior a position. (3) Inability of an impaired cardio-circulatory-respiratory system to withstand the excessive demands made by a convulsion.

Group 3 is clearly the one into which most but not all cases fall.

Some of the individual deaths seem worthy of special comment. The case of the ruptured intestine occurred in a man of 28 years, an impulsive, aggressive schizophrenic. He was given one treatment with no unusual reaction. Forty-eight hours later the nurse reported that he appeared physically ill. At operation he was found to have a tear one and a half inches long in the upper ileum and a small half-inch tear retroperitoneally in the third part of the duodenum. The pathologist said: "The cause of death was toxæmia due to general peritonitis following rupture of small intestine. There would not appear to be any reason for the condition other than the electrical treatment administered to the deceased." I do not know of any similar occurrence.

The case of fat embolism occurred in a depressed woman of 58 years. She received 12 shocks in 1944 and was discharged recovered after three months. She was readmitted in 1949 and was treated with E.C.T. but twenty minutes after recovering from her third treatment she became cyanosed and died. The pathologist said: "Death in this instance must be related to convulsive therapy which produced fat embolism in the small vessels of the brain and so interfered with vital centres."

The only thoroughly investigated case of cerebral fat embolism causing death with E.C.T. is that reported by Meyer and Teare (1945). These two appear to be the only cases of fat embolism known as a complication of E.C.T.

The hæmorrhage in the internal capsule occurred in a schizophrenic man of 48 years. During his second treatment crepitus was heard in left shoulder. After recovering consciousness he was found to have a stellate fracture of the left scapula, two hours later he fell to the floor with a convulsion, and died without recovering consciousness. The post-mortem showed a large cerebral hæmorrhage in the internal capsule. The Medical Superintendent thought that treatment and hæmorrhage were coincidental.

Another case of cerebral hæmorrhage occurred in a woman of 57 years suffering from anxiety and depression who was given one treatment. Forty minutes later she drank a cup of tea. Ten minutes later she collapsed and died. The doctor had given 5,000 treatments in two years without mishap. The pathologist stated: "In the R. cerebral peduncle and in the right side of the pons there was an area of punctate hæmorrhage 3 mm. in diameter. This could be traced down to the upper part of the medulla where it consisted of a single hæmorrhagic streak 1 mm. in diameter. The most probable cause of this condition was the E.C.T. although we cannot rule out completely that the condition might have been coincidental." One case may be a coincidence but two make it much less likely.

The occurrence of cerebral catastrophes which can be attributed to E.C.T. is rare. Apart from the three which I have mentioned and the case of cerebral fat embolism reported by Meyer and Teare I could only find six other reports which were convincing. Will *et al.* (1948) reported one death which they attributed to acute cerebral œdema and medullary compression. Riese (1948) reported 2 cases with histopathological changes: in one there was œdema and punctate hæmorrhages in the medulla with marked cellular changes; in the other there was hæmorrhage in the meninges and many small areas of necrosis. In 1949 Riese and Fultz reported a case of shock treatment followed by complete flaccid paralysis, hallucinations and death. The central nervous system showed fatty products in the nerve cells disseminated through all levels. In 1951 Liban, Halpern and Rozanski reported a case in which there was widespread thrombosis of the sinuses, subdural and subarachnoid hæmorrhages and areas of hæmorrhagic softening in the thalamus and cerebellum. This occurred in a man of 47 who died two days after his seventh treatment. In Belgium Dumont *et al.* (1946) reported a case of subarachnoid hæmorrhage after electro-shock treatment.

Professor Meyer (personal communication, 1952) has allowed me to mention one other interesting case, which has not been published, of cerebral embolism in a woman of 28 years who had an underlying subacute rheumatic heart disease without clinical symptoms. The embolism occurred immediately after the second E.C.T. Histological examination showed small vegetations on the cusps of the mitral valve. In a few places corresponding to the vegetations the endocardium was lost and the underlying tissue showed evidence of recent hæmorrhage. In the brain there was a considerable area of recent softening on the right side involving the basal ganglia, insula and adjacent regions of the temporal and parietal lobes (Figs. 1 and 2).

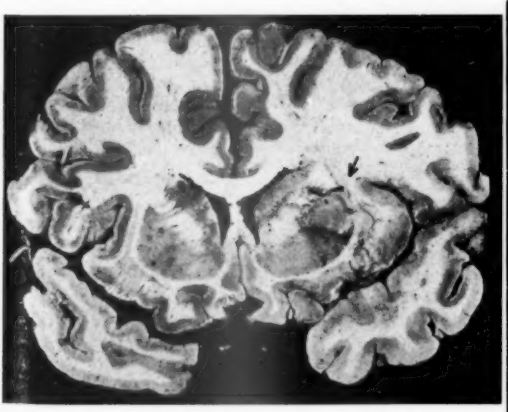

FIG. 1.

FIG. 2 ×1·6.

FIGS. 1 and 2.—*Cerebral embolism.* Note the softening on the R. side involving basal ganglia, insula and adjacent parts of temporal and parietal lobes. Underlying condition was subacute rheumatic heart disease without clinical symptoms. Embolism occurred immediately after E.C.T., the embolic softening shown in a slide stained for myelin.

These cases show that irreversible cerebral damage can be caused by E.C.T. but leave unanswered the question of how much of the damage is due to the current and how much to the effect of the convulsion.

One of the deaths reported by Napier in 1944 was due to massive hæmorrhage in the thyroid gland. This is my excuse for mentioning that in three instances in my series there were thyroid adenomata present, with varying degrees of toxicity. They are not of any special significance but one object of the investigation was to look for coincidences that might be even remotely suggestive. In one of these cases the pathologist did report death as due to E.C.T. contributed to by latent thyroid disease. The patient was a woman with an extensive adenomatous goitre with areas suggestive of toxicity. She had had a hard time. The doctor stated that "it was found necessary to give E.C.T. as a maintenance treatment since, if it was stopped, she became noisy and excitable". She was given 103 treatments before she gave up trying and died.

Another interesting patient was a 39-year-old male schizophrenic with mental defect. After his first treatment he had fractures through the necks of both femora and died next day of acute pulmonary œdema. One wonders if this may not have been another case of fat embolism. Post-mortem examination of the bones showed no abnormal fragility. The bones were completely severed and the necks had been driven into the medullary cavity of each head with great force. I know that accidents can occur. None the less, one or two of these cases raised doubts about the skill with which the treatment was given. I remember investigating an alarming number of fractures of long bones in one hospital. The reason appeared to be the therapeutic enthusiasm of a new medical officer who had failed to appreciate that many of the patients whom he wanted to help were elderly and had been kept in bed for a long time, possibly with a diet that was not entirely adequate, and that their bones were excessively fragile in consequence.

2 of the 3 patients who died of pulmonary embolus had thrombosed veins in their legs at the time of treatment. 2 other instances of pulmonary embolus from this cause occurred—one in a restless patient under continual narcosis, the other in the leucotomy series. It is a clinical observation worth bearing in mind.

There were 4 instances of patients dying before the convulsion was given. One was a depressed woman of 52 years with a large thyroid adenoma, tuberculosis of the spine and a quiescent tuberculous lesion in the right lung. She had two uneventful fits and died at the third before the fit was given following premedication with atropine, morphine, cyclonal sodium, Flaxedil and Dexedrine. The pathologist reported that there were pin-point hæmorrhages on the anterior wall of the fourth ventricle and in the substance of the medulla. Another was a depressed woman of 53 who had had seven treatments with E.C.T. and C 10 in 1949 and made a good recovery. She relapsed in 1951 and it was decided to give E.C.T. although she had bronchiectasis. She was given hyoscine and Flaxedil and died before the first treatment. The third was a woman of 42. In 1948 she was given 4 convulsions but was found to have a fracture of the right shoulder. In 1951 it was thought wise to try again with a relaxant as her mental state was so bad. Flaxedil and sodium amytal were used. The patient's breathing failed and she died twenty minutes later without a convulsion having been given. The pathologist found chronic thickening of the pleura on the left side and the lung shrunken in size; he stated as causes of death: (1) "Pulmonary œdema and congestion caused by paralysis of muscles of respiration due to injection of Flaxedil and sodium amytal. (2) Fatty degeneration of heart and liver."

The points that these 3 cases have in common are (1) that they all had pathological lung conditions and (2) that Flaxedil was the relaxant used. The fourth was a man of 63 who died following injection of Tubarine and Pentothal.

In most of the cases where a risk had been recognized and accepted relaxant drugs were used to diminish the risk but I am not sure that the dangers as well as the advantages of relaxants were always recognized; some of the records suggested that they were not. Indeed the whole subject of premedication and relaxants seems to need more research as the advice given by experts is very variable. Will and his colleagues (1948) say: "The cardiovascular system is placed under considerable strain by the blood pressure variations that occur and by the anoxæmia incident to the post-shock apnœa. The alterations in blood pressure are not eliminated by the use of curare and the period of apnœa may be prolonged by using it with resultant hypoxæmia of the cardiac muscle." Jones and Pleasants (1943) say: "It is becoming apparent that curarization is to be used most cautiously in severe cardiac disease, since the period of apnœa may aggravate myocardial changes from sclerotic vessels." We have already seen that in this series there were 22 cases of cardiac failure and 10 of coronary occlusion, including a case of rupture of the heart wall in a man of 64 who had received premedication with hyoscine and Scoline. On the other hand Bennett (1949) says: "In over 20,000 treatments we have had no accidents we could attribute to curare." Again, Altschule and Tillotson (1948) point out that atropine is dangerous with curare because it blocks neostigmine but Hejtmancik and his colleagues (1949) recommend large doses of atropine thirty minutes before curare and E.C.T. to avoid cardiac arrest. In January Esplen (1952) advocates the use of thiopentone, in February Beresford Davies (1952) points out its dangers. Perhaps the new short-acting relaxants are going to be an answer to some of our problems but Mayerhofer and Hassfurther (1951) have shown how variable is the sensitivity to synthetic curare, and the same may be true for them.

Of the 62 patients who died 28 had received a relaxant and other premedication. The variety of combinations and permutations in the use of the various relaxants and various drugs made any attempt to find whether any combination was more dangerous than another quite futile. The problem was further complicated by the various techniques used in giving the shock treatment.

None the less some of the cases do arouse a suspicion that the premedication had something to do with the death. To begin with there are the four already mentioned who died before the fit was given. Then there was a woman of 71 who received 20 applications of E.C.T. in two years. Her blood pressure was rising, so, after careful consideration, she was given hexobarbitone and curare prior to E.C.T. and died after the first treatment. A woman of 27 was given a course of E.C.T. successfully but when given E.C.T. plus curare died after the third treatment. A man of 66 had five short courses of E.C.T. but died at the first treatment with curare. A man of 61 with bronchiectasis was given E.C.T. on four occasions, on the fifth he was also given Eulissin and died. The pathologist said: "Deceased who was under the influence of Eulissin was clearly unable to clear his air passages and collapse of the lungs has resulted." A woman of 42 had 4 shocks in 1948 but fractured her shoulder, so in 1951 she was given sodium amytal and Flaxedil, when she died. The pathologist reported: "Death due to pulmonary œdema and congestion caused by paralysis of muscles of respiration due to Flaxedil and sodium amytal." These cases make one wonder if relaxants are an unmixed blessing. I am inclined in particular to agree with those who say that relaxants should be used cautiously in cases with cardiac complications. I am certain that more research is needed in this field of the type reported by Thompson and Norton (1951) or Smith and Thomas (1951).

Information about the number of convulsions received was available in 54 cases and is shown in Table IV.

TABLE IV.—NUMBER OF CONVULSIONS GIVEN DURING FATAL COURSE OF TREATMENT

Number of convulsions	1	2	3–9	10–20	over 20
Number of patients ..	26	6	16	5	1

The main point of interest is that half the deaths occurred after the first convulsion. In Will's series the proportion of deaths after the first shock was also high, 8 out of 25, but not so high as here.

Electronarcosis was responsible for 5 deaths but the post-mortem examinations and reported causes of death throw little or no light on the mechanism involved. One, a girl of 21, had a full course of E.C.T. She was later given five treatments with electronarcosis but at the sixth died of "cardio-respiratory failure with collapse of both lower lobes"; another aged 34 had two successful treatments and died after the third due to "shock caused by the effect of treatment in vital nerve centres"; a man of 31 had two courses of E.C.T. and three satisfactory treatments with electronarcosis then died after the fourth of "medullary failure"; nothing was found post mortem. A fourth aged 56 had two courses of E.C.T. then died after his seventeenth electronarcosis treatment; death was said to be due to "cardiac arrest". The fifth died after eighteen treatments of "central cardio-respiratory failure". There is little to help us in these reports. Meyer and McLardy (1950) investigated 2 cases where death occurred during the fourth and fifth fits respectively and found no structural changes of any significance. Alpers and Madow (1948), however, reported one death with diffuse recent hæmorrhages occurring at the first treatment.

LEUCOTOMY

During the years under review there were about 180 deaths directly resulting from the operation of leucotomy in mental hospitals. The number of operations was between 8,000 and 9,000 giving a death-rate of approximately 2%. This has remained fairly constant over the years and is in accord with results elsewhere.

A hundred case reports were examined but the results do not seem to add anything to already existing knowledge and will be only mentioned briefly. There were a few more women than men. The age distribution is shown in Table V, and causes of death in Table VI.

TABLE V.—AGE DISTRIBUTION OF LEUCOTOMY DEATHS

Years	19–25	26–35	36–45	46–55	56–65	66–75
Number of patients	8	27	20	20	14	11

TABLE VI.—CAUSES OF DEATH FOLLOWING LEUCOTOMY

Cerebral		*Respiratory*	
Cerebral hæmorrhage	56	Bronchopneumonia	12
Cerebral abscess	5	Pulmonary embolism	5*
Subdural hæmatoma	1	Collapse of lungs	2
Acute suppurative encephalitis	2	Asphyxia (due to inhalation of vomit) ..	1
Post-operative cerebral softening ..	2	Cardiac failure	4
Cerebral œdema	1	Surgical shock	3
Cystic degeneration of frontal lobes ..	1	Post-operative coma	1
Convulsions	3	Uræmia, with pyelonephritis	1

* 1 rheumatic heart, 1 femoral thrombosis.

It is apparent that the main immediate danger of the operation is hæmorrhage and that, as yet, no way has been devised completely to avoid it.

I must at this stage mention another direct but not immediate cause of death from leucotomy which is not revealed in my information. I refer to the "delayed operative deaths", described by Meyer and McLardy (1948 and 1949) due to posterior cuts, i.e. cuts involving the posterior half of the orbital region, the striatum, the premotor area, the region of the external capsule or any combination of these. McLardy (1950) deduces from a study of the brains and clinical records of 101 leucotomy cases that probably as high a proportion of the leucotomized population dies a "delayed operative death" from uræmia or marasmus within five months of the operation as from hæmorrhage within two weeks. He concludes by saying: "The practical intention of the paper is to emphasize the serious danger of 'delayed operative death' from the use of blind leucotomy techniques, including the 'deep' transorbital cut."

I am unable to express any opinion about these findings or about the "deep" transorbital cut but in 7 of my cases where hæmorrhage was the cause of death the operation was done by the transorbital route. I mention this because Freeman (1949) says: "Transorbital lobotomy is simple, quick and safe. It is recommended particularly for psychiatrists in mental hospitals." Fleming and Phillips (1949) say: "The danger of serious damage to intracranial blood vessels with this blind operation appears to be small." On the other hand Oltman *et al.* (1949) report 4 deaths in 107 patients, and McKissock (1951) condemns the operation saying: "The whole technique offends established aseptic surgical principles." I do not want to condemn the operation but only to point out that it is not so safe as some of its protagonists make out.

Not all the leucotomy operations were done by neurosurgeons. In my opinion they should be. Apart from the danger of the operation I believe that it is only by the application of trained and skilled minds to the problems of leucotomy that advances will be made in technique and knowledge. The only exception that I would make is when it is impossible to get a neurosurgeon and the patients are being deprived of the benefits of treatment; then one must do what one can, but it should be a last resort even if the results appear to be satisfactory.

I think that it is permissible to mention as a possible lethal complication of leucotomy three murders committed by leucotomized patients who are now in Broadmoor. There is, however, little or nothing in their histories to suggest that the operations released impulsive actions which were not already overt, though they did nothing to subdue them. One is a man of 35 who developed a catatonic schizophrenic illness at the age of 29 years. He struck a woman in the street under the influence of "voices". In his first mental hospital where he had insulin and E.C.T. he was regarded as violent and hallucinated. After operation he was destructive, violent and incoherent. He attacked fellow patients more than once and finally killed one.

The second is a woman of 32 years who had been regarded as a morally defective aggressive psychopath. As a child she was treated for a violent and uncontrolled temper. She graduated through an Approved School and Borstal to a mental hospital where leucotomy was performed. She absconded and lived the life of a tramp till she had a quarrel with an old man in a bomb shelter and killed him.

The third is a woman of 38 years of superior education and intelligence. For many years she was subject to migraine and to phases of depression with hypochondriasis and obsessional thoughts and actions. She received a great deal of psychotherapy and other psychiatric treatment culminating in leucotomy, all without benefit. She then murdered her daughter and attempted suicide.

As I have already said, it is possible that leucotomy may have influenced the conduct of these patients but their previous history does not suggest that it did do so.

Insulin

The number of deaths due to insulin treatment of schizophrenia was 44, 24 males and 20 females. The age distribution is, as might be expected, in sharp contrast with the E.C.T. deaths. 36 were under the age of 35 and only 2 were over 55 years. Table VII gives the reported causes of death.

Table VII.—Causes of Insulin Deaths

Irreversible coma	13
Epileptiform convulsions	7
Subarachnoid hæmorrhage	1
Asphyxia (one with enlarged thymus)	2
Asphyxia due to inhalation of vomit	3
Acute pulmonary œdema	7
Pulmonary collapse	2
Bronchopneumonia	1
Cardiac failure	5
Coronary thrombosis	1
Cardio-respiratory paralysis	1
Anaphylactic shock	1
	44

Tables VIII and IX show the number of comas and the dosage of insulin in those cases where information was given.

TABLE VIII.—NUMBER OF COMAS BEFORE DEATH

Number of comas	1	2	3	4	5–10	10–20	20–40	Over 40
Number of patients	4	3	3	1	2	7	7	nil

TABLE IX.—DOSAGE OF INSULIN AT TIME OF DEATH

Units of insulin ..	0–50	50–100	100–200	200–300	300–400	400–450
Number of patients ..	2	4	9	5	3	3

In respect of irreversible coma these findings are in accord with the views of Rivers and Rome (1944) that age, sex and insulin dosage are not significantly related to prolonged coma but that the decisive factor is the total reaction at a given time.

In insulin treatment even more than in other physical treatments avoidance of complications depends on skilled supervision; and better understanding of the complications that do occur depends more on detailed research on individual patients than on the kind of information that comes to me.

CONTINUOUS NARCOSIS

There were 8 deaths during courses of continuous narcosis. All except one, a man of 70 years, occurred in comparatively young patients between the ages of 25 and 45 years. Most of the deaths occurred towards the end of the course of treatment which suggests that the medical care and nursing throughout treatment by continuous narcosis should be strict and unremitting. The causes of death were respiratory in 4 instances, cardiac failure in 3 instances and unknown in 1.

MALARIA TREATMENT SURGICAL OPERATIONS ANÆSTHETICS INTRAVENOUS INJECTION DRUGS FOR EPILEPSY

There is little that is relevant to say about the 6 deaths due to malaria treatment or the 6 deaths after operation.

Nor is there much to say about the 13 anæsthetic deaths except a reminder that there is a risk of death even in minor procedures for the 13 include operations for incision of a whitlow, removal of toenail, hæmorrhoids, bronchoscopy, lumbar puncture, cataract, cystoscopy, stricture and paracentesis. In 9 instances the anæsthetic was thiopentone, an anæsthetic that is apt to be used a little light-heartedly because of its comparative safety.

Indeed the whole question of anæsthesia and its complications as a precipitating cause of personality changes, prolonged confusion, psychoses, dementia and accelerated death is in need of attention. Meyer and McLardy (1950) say that anoxic catastrophes due to anæsthetics have not yet been accorded the attention which they merit. Anoxia can be caused by E.C.T. and relaxants as well as by anæsthetics and as patients often receive all three together it seems clear that here is a complex problem requiring skilled study.

Two of the deaths due to intravenous injection followed the intravenous injection of T.A.B. vaccine intended for subcutaneous use. The third was an allergic reaction after intravenous injection of N.A.B.

The 2 deaths due to drugs for epilepsy occurred in mental defectives. One was due to a toxic hepatitis following a severe reaction from a blood transfusion given as treatment for agranulocytosis after Epanutin and Mesontoin. The other was due to hepatitis following the use of 0·3 gramme of Tridione twice a day for three months.

PSYCHOTHERAPY

No deaths have been reported to the Board of Control as due to psychotherapy, but we have all been taught and have even taught others about the dangers of, for example, analytical treatment in unskilled hands or in inappropriate cases. One would therefore expect to find instances where unskilful or unwise therapeutic interference had precipitated catastrophes such as suicide or murder. Over 20 psychiatrists experienced in psychotherapy were questioned but to my surprise I could only get two rather dubious instances. Whether this means that psychotherapy is less dangerous than is commonly supposed or whether psychotherapists always choose and treat their patients with unfailing skill or whether the mechanism of rationalization is disproportionately developed in psychotherapists I must leave others to judge.

DISCUSSION

Is the use of empirical methods of treatment justifiable in that they do have a mortality rate, though a small one, and are not used as urgent life-saving procedures? I believe that their benefits far outweigh the disadvantages, provided that they are used with due consideration of the needs of the patient, due assessment of the possible complications—of which death is only one—and provided that they do not lead the psychiatrist to neglect the patient's personal problems.

I know, too, that as a result of the use of treatments such as E.C.T., insulin and leucotomy, hospitals are much pleasanter places both for the patients and for the staff who work in them.

Perhaps most important is to compare treated with untreated patients. I shall not deal with the questions of recovery and improvement or length of stay in hospital. I shall adhere to my subject of death but now with a more cheerful bias as I think it probable that these treatments prevent a great many more deaths than they cause. The effectiveness, for example, of E.C.T. in preventing death is supported by Slater (1950). In a paper discussing the results of E.C.T. as evaluated by Karagulla (1950) he showed that among the untreated groups the proportion of persons who died was about eight times as great as the proportion of those who died in the treated groups.

Its value in preventing suicide is supported by various workers. Huston and Locher (1948) showed that in a group of patients suffering from involutional psychoses there was 7% of suicides in those treated without E.C.T. but only 1% among those who received it. Fetterman *et al.* (1951) state that of the 100 treated patients whom they followed up for ten years not one committed suicide though prior to treatment 15 had made suicidal attempts. On the other hand out of 10 patients who did not receive E.C.T. 3 committed suicide.

Professor Polonio of Portugal (1951) has published the results of a careful ten-year follow-up comparing 500 patients treated with insulin and E.C.T. with a control group of 500 patients. In the former there was a death-rate of 13·5% compared with 31·9% in the latter. In the manic-depressive patients the death-rate was 4·1% in the treated group compared with 18·9% in those treated by other methods.

In this country the deaths in mental hospitals due to G.P.I. dropped from 1,353 in 1923 to 164 in 1948 following the introduction of malaria treatment.

Conclusion

I appreciate the desire of doctors to be active in relieving human suffering, a desire which may indeed be emotional rather than intellectual or scientific but which, even if it subserves a personal need, is good and even necessary in those who care for other human beings; but a doctor by the very nature of his work must be a responsible person with a proper sense of values, able to decide what is the best treatment for his patient and free to apply it. In doing so he must know the dangers as well as the benefits of being either active or passive so that he can assess them wisely. A psychiatrist, because he so often has to deal with patients incapable of making their own decisions, has an even greater responsibility to bear in this respect and must accept it.

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Section of Surgery

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[*October* 1, 1952]

The Surgeon and His Environment

PRESIDENT'S ADDRESS

By Professor F. A. R. STAMMERS, C.B.E., T.D., Ch.M., F.R.C.S.

IN the busy routine of surgical practice we do not ordinarily have much cause to give thought to the environment of our activities.

I first began to think about environment and its influence on surgery when trying to analyse and explain for myself the difference between British and American surgery as I found it when spending the whole of 1929 in the States. I thought much more about it in the weeks following Munich when, like many others, I committed myself to the R.A.M.C. should war come. Another experience that made me realize the profound influence of environment on surgery was contact for two years with the Colonial Medical Service in West Africa, to which was added a sort of refresher acquaintance with this Service and with work in backward countries during a lecture tour in Middle East earlier this year. Finally, as the one responsible for the organization of the teaching of surgery in Birmingham, I have to have some objective concerning the development and functions of a whole-time unit in respect to the treatment of patients, the teaching of students, the training of young surgeons, and the prosecution of research.

I should, therefore, like to discuss environment under three headings: (1) War Surgery; (2) Surgery in backward countries; (3) Surgery in Great Britain, having regard to modern trends.

I.—WAR SURGERY

In the Official History of the Army Medical Services of the First War is to be found the finest and most complete account ever written on the fight against sepsis. This is not the time or place to go into details, but only to point out that the surgeons, bacteriologists and pathologists of the day discovered that excision of wounds was the surest way of preventing gas gangrene, spreading cellulitis and smouldering osteomyelitis; they learnt that dead muscle bred gas gangrene and that pieces of indriven clothing and equipment were more dangerous than metallic fragments; they discovered the possibility and value of delayed primary suture; they realized that a stitched wound subjected to trauma of an ambulance journey over rough roads became inflamed. All this was done without sulphonamides, antibiotics or readily available blood. But why did these wounds behave so differently from those of civilian trauma? It was the whole environmental circumstances—trench warfare in cold, wet weather, when men wore many thicknesses of clothing soaked in the liquid mud of a highly cultivated soil; missiles of jagged pieces of metal carrying in with them highly infected pieces of clothing; exposure; continuous hazard; delay in getting patients to surgical centres.

All this is admirably recorded in the Official History, and its study gave a pretty clear idea of what we might expect in the Second World War, though we had not, at that time, learnt to appreciate that different operational areas might give different environments, possibly with medical repercussions.

It was somewhat disconcerting, therefore, when Trueta's book on his surgical experiences during the Spanish Civil War, published in 1939, strongly advocated the closed and unpadded plaster treatment of war wounds. He excised wounds as the First War surgeons did, but there was no mention of delayed primary suture. To those who had served in the First War or who had read the Official History, this closed plaster method seemed dangerous. The explanation lay in the fact that Trueta's cases were picked up off the streets of Barcelona and were in hospital within an hour or so, thus being

spared the continued trauma suffered by men wounded in the open field of battle. During the Second War these fears regarding the use of plaster were amply confirmed, and it became an inflexible rule that no unpadded plasters be used, and that circumferential plasters were always split before transportation.

In 1942 I was appointed Consultant to Western Command, and as such attended the monthly Consultants' Committee at the War Office. Again, one was puzzled since, at about this time, memoranda on the treatment of wounds were arriving from M.E. declaring that their experience had proved that excision of wounds as understood in 1916/18 was unnecessary and, therefore, mutilating, and that it should cease; and this satisfactory behaviour of wounds was attributed, not unnaturally, to the new tool, the sulphonamides. These memoranda were all the more disconcerting since they coincided with reports coming from Sicily that wounds were behaving as they had done in North Africa, and before that in France during the brief fighting in 1940, and that without adequate excision spreading cellulitis and septicæmia were occurring.

How could all these contradictory experiences and reports be reconciled? There is no doubt that it was a matter of different and changing environments, of which the dominating factors were climate, terrain, and communications. I believe it should be possible in any future war to foresee and plan the optimum management of casualties according to the particular set of environmental circumstances of the moment. In other words, the management of wounds is not rigidly standardized for all circumstances. Warfare over cultivated soil in the cold, wet season, particularly if there is delay in getting casualties to a surgical centre, demands thorough excision of wounds: in desert warfare, where contamination is relatively slight because the men wear a minimum of clothing, and the soil is not cultivated, a technique of the snip and trim variety is sufficient. In either case, where it is possible to organize adequate centres to which cases can be delivered by the fourth to sixth day after wounding and held for a further eight to ten days or more, delayed primary suture should be universally employed, as it was in Italy. As I have said, it was used in the First War and again by individual surgeons during the Second, but not until the Italian Campaign did easy communications make it possible to adopt the method universally, a fact that Harold Edwards was quick to appreciate and, in consequence, urged the necessary organization at Base for its use as the standard second stage treatment of wounds. Skin cover is the best dressing, and in the 85–90% cases in which primary healing takes place, delayed primary suture converts fractures to simple ones, and excessive scarring of soft tissues is prevented. Also, it is safe to use closed plasters when cases can be held from the moment of surgical treatment, but, once evacuation is necessary, those plasters must be split.

This brief account over-simplifies the problem, for in front of this background of climate, terrain and communications are additional frequently changing local factors such as road blocks, a burst of enemy activity, a static phase giving place to one of movement, the arrival of a new and inexperienced unit. All these things have their medical repercussions.

With all these experiences behind us, one would have thought it impossible for similar errors to be repeated. Yet when I was in America two years ago I was taken by Dr. Churchill, one time Consultant to the American Forces in C.M.F., to see some newly arrived casualties from Korea. They had been wounded nine to fourteen days previously, and had been flown by stages to the nearest Service Hospital to their homes. They had travelled excellently, and their wounds were clean; but not a single one had been treated by delayed primary suture, a method which had paid such handsome dividends only six and seven years previously. A few days ago I had a long conversation with one of our Birmingham men who had just returned from two years in the Far East, and I was glad to hear that delayed primary suture had once more become the policy of the day. But there it was again, environment dictates every time, and even the most up-to-date surgeons are forced back to what has been proved twice in our own lifetimes.

II.—Surgery in Backward Countries

For two years during the early part of the war I served with the 34th General Hospital in Freetown, Sierra Leone, and so was able to learn at first hand much about this excellent Service and what surgery in the tropics really meant. The climate is characteristic of coastal places in the tropics, with temperatures never above 97° F. and rarely below 75° F., and great humidity most of the year, rising to about 95% in the two wettest months. In early January it is delightful, but the rainy season, from about May to September, is very enervating. The mere action of walking across the room causes profuse sweating from the back of the hands and forearms, and the operating theatre was really unpleasant; and, of course, there was no air-conditioning. We had been warned not to operate during the rainy season, since wounds healed badly, but we found that healing was satisfactory provided that bulky dressings were avoided since they caused sweat rashes, and we found the "cracker" dressing particularly suitable. Fluid intake was large, the average man lying in bed following a simple operation, such as for hernia, requiring 7–10 pints daily. Even then it was no uncommon thing for patients getting up for the first time after, perhaps, ten days in bed, to complain of bilateral pain from loin to groin, frequency, and the passing of urine loaded with urates and phosphates. As a corollary, particular care was necessary with the sulphonamides, since the only ones then available were sulphanilamide and sulphapyridine, and the renal pelvis and ureters might become blocked by acetylated derivatives.

All natives and most white men had had malaria, and this, at first, caused us anxieties because trauma and severe fatigue would very often precipitate an attack. A man having sustained a simple fracture, or having undergone a simple operation, might develop malaise and high temperature, perhaps with vomiting, two days later, and this was very worrying and puzzling until we learnt that examination of a blood film almost always solved the mystery. At a later phase of the war I learnt that troops having served in malarious areas previously, not infrequently developed malaria afresh following a wound during a landing assault elsewhere. A number of such cases were encountered in Sicily, and unconsciousness following head injuries was sometimes found to be the result of cerebral malaria rather than concussion. Another result of climate was that abnormalities such as varicose veins and hallux valgus, never having given trouble before, quite genuinely caused severe discomfort in this humid climate. In peacetime the Colonial Services get leave from West Africa every fifteen months, and after serving there for twenty-two months, as some of us did, one could see why, since one loses energy and feels vaguely dispirited, with no initiative or enthusiasm, if there too long.

We had some first-class British sisters and nursing orderlies, but as we expanded we began to train native orderlies, and this presented difficulties, since not all could read or write, and their sense of ethics did not prevent them from demanding cash before handing out drugs ordered by the M.O.s, or even bedpans. And in a country where 70% of males suffer from V.D., it was discovered that sulphanilamide tablets were disappearing from the medicine cupboards only to reappear elsewhere at 6d. a tablet.

The language difficulty was great, for there are many different ones in Sierra Leone. Histories often had to be taken through not just one interpreter but through a whole series, and it was wellnigh impossible to elicit any detailed story. A simple question would be followed by long, lively and gesticulating conversations all along the line to the patient and then back again.

Venereal disease is very common, and all six types are met with in West Africa, often several concurrently. The most interesting ones were, firstly, lymphogranuloma inguinale (L.G.) and, secondly, yaws. L.G. is a virus infection with a fleeting primary lesion on the glans penis followed about three weeks later by enlargement of the inguinal glands. These might remain chronically enlarged or they might break down, producing sinuses becoming secondarily infected. In females the infection passes from the vagina back into the rectum giving rise to stricture and fistulæ. Occasionally, the rectum becomes infected in the male, and later on in the war, I was intrigued to see a regular soldier in the military hospital in Manchester with stricture of the rectum, enlarged inguinal glands and a positive Frei's reaction. The more usual form of L.G. is not uncommonly seen in merchant seamen in port town hospitals. Yaws has as many manifestations as syphilis and is thought by some to be the tropical form of the latter. One form was of special interest to us. The victim complained of symptoms not unlike muscular rheumatism or fibrositis in a limb, and on examination some tenderness and possibly some thickening could be found. X-rays revealed periosteal reaction and subperiosteal new bone, not unlike a low-grade osteomyelitis, but not confined to the ends of the bones. The Kahn or Wassermann test was positive. These cases all responded to iodides and arsenicals. Another form was an affection of the tendons and sheaths giving ganglion-like swellings which, on exploration, revealed a curious yellow gelatinous degeneration of the structures involved. The other tropical diseases with which we had to deal were pyomyositis, filariasis, bilharzia, guinea-worm, onchocercus volvulus, loa-loa, tumbu-fly: and tropical ulcer was so common as to be a real man-power problem. These ulcers occurred on the feet and lower parts of the legs of the unshod African soldier, and were the result of trauma to which was added a heavily mixed infection which the humid heat tended to foster. Shortly after our arrival we were asked to work out a last for a boot for the native soldier. The widest part of his foot is at the tips of his toes, not at the metatarsal heads, and the skin and subcutaneous tissues of the sole are immensely thick, so the British Army boot was useless.

After we had been there a few months we were asked to run the surgical side of the Government Hospital for three months whilst their surgeon was on leave in South Africa, and this experience added greatly to our understanding of the environmental circumstances of surgery in backward countries. The hospital was pleasantly situated and the wards large and airy. The sisters were British, but the nurses were native. As in so many backward countries, it is difficult to persuade the few educated women to take up nursing, and the ones we had were slow, not very intelligent, and in a constant state of weariness, probably a direct result of the climate and of malaria. It would be impossible to rely on them for skilled pre-operative preparation or post-operative care, and anything like fluid charts or the supervision of intravenous drips would be quite beyond them. Anæsthetics were given by the native pharmacist—simple rag-and-bottle methods, or ethyl chloride out of a closed inhaler, very well given but quite inadequate for modern surgery. Amongst civilians we met lympho-granuloma inguinale in the female, with all the rectal and pelvic complications this disease produced; also filariasis, not only the dramatic elephantiasis variety, but other forms, as it affects the peritoneum and the vaginal sac of the testicle. There were many cases of breast cancer, and large ovarian cysts and fibroids. There were also many fractures, lacerations and septic hands, and a great variety of genito-urinary cases, particularly the sequelæ of venereal disease. There was no X-ray therapy machine, a miss of no great importance, since the up-country native's mind thinks only in terms of kill or cure, and palliative measures play little part in treatment.

From this two-year experience it is clear that the general environment of West Africa demands surgery of a jack-of-all-trades type, with particular experience in traumatic and genito-urinary work; that a considerable number of entirely different diseases are to be encountered; that the climate and primitive standard of living and the philosophical outlook of the majority of natives modify considerably their psychological and physical reaction to sickness. Superstition is very near the surface, and one feels that the witch doctor with his bones, charms and incantations is only just round the corner.

I had assumed that the nursing staff difficulties, the simplicity of anæsthesia and the absence of any blood transfusion service were repercussions of the war. But a lecture tour in Middle East last March revealed that, at any rate, so far as Cyprus, Baghdad and Khartoum are concerned, the same conditions still hold. In Cyprus I found a very highly skilled senior surgeon doing all his gastrectomies under local and spinal anæsthesia because the only skilled anæsthetist was on the other side of the Island. At the same time, the physician in charge of a beautiful little modern sanatorium in the mountains, who performed his own thoracoplasties very skilfully, also did them under local anæsthesia which, of course, is a good thing, but for the same reason he could not attempt segmental resection which is often the better treatment. Baghdad and Khartoum were both desperately short of nurses. As a rule, there is a British Matron and a nucleus of British sisters, but without them it is difficult to see how a service could be run. Nowhere was there a transfusion service—they are in the same position as we were thirty years ago, sending for relatives and neighbours and testing until a suitable donor is found.

The public health side of the Colonial Medical Service will always save more lives than surgery, and it is obvious that surgery in backward countries must be practical and straightforward, without frills or exotic exercises; but since some surgery, at least, is required, it needs to be done under proper circumstances. When administrators have, from their own personal experience, a wide knowledge of surgical activities, and take a lively interest in surgical advances, particularly those of real practical value to backward races, I am satisfied that they will see to it that progress is made possible and is encouraged to march at a tempo suitable to the country concerned. But in less fortunate countries, I should fear that enthusiastic young surgeons, having watched the enormous strides that have been made since the war, might find a lack of sympathy towards their endeavours to improve things and then feel frustrated, finally slipping into a groove of stagnation. On the other hand, I realize that enthusiastic young surgeons are liable to want to do things that are not necessarily useful to backward peoples. Whatever be the solution, no real forward move is possible without reliable nursing, good anæsthesia, and the semblance of a transfusion service.

III.—Present-day Surgery in Great Britain

Coming now to surgery of today one realizes that its quality and organization are very different from, say, thirty years ago, and that the environment in which it is practised has changed completely. It is probably correct to say that at the turn of the century few medical schools, certainly no provincial school, had more than two or three really good, progressive surgeons—the rest were mediocre, often general practitioners. But these two or three were regarded in their own locality as little gods, and they were powerful personalities and profound individualists but fine clinicians and first-class technicians. Our own teachers were brought up by these giants, who in my own School were such men as Lawson Tait, Joseph Sampson Gamgee, Furneaux Jordan and Jordan Lloyd, and it is not surprising, therefore, that they, too, were strong individualists. They were jacks-of-all-trades, doing, as Charles Mayo once said, "anything from corns to corneæ, with all the intervening territory", though it must be said that operations were fairly simple and lists not often more than two to three hours in duration. Gynæcology, and Ear, Nose and Throat work had just split off, but for the rest, everyone took his share of bellies, amputations, genito-urinary cases, heads, chests and fractures.

Medical and surgical firms corresponded rigidly for consultative work, and any deviation from this custom would have been regarded as little short of disloyalty and a veiled insult. Not until Moynihan started a travelling surgical club, out of which grew the Association of Surgeons of Great Britain and Ireland, did any but the very few visit other Centres to find out what others were thinking and doing, and almost nobody went abroad for more than a few days. There certainly were no funds to enable any young surgeon to study in another country. Hospital laboratories were meagre affairs, and only for routine work, and there were neither technicians nor even bench space for any young enthusiast with time on his hands to study a problem and work out things for himself. Hospital funds were always strained, and it was difficult or impossible to get apparatus or new instruments, certainly for a junior. Anæsthetics were of the rag-and-bottle variety, and patients might have to be wheeled from the theatre to their ward across an open courtyard. There was no blood transfusion service, and little knowledge of water and crystalloid balance.

In my own student days the Staff were all men of great practical experience and first-rate technicians, but anything they might throw light on or discover tended to die with them, for they published little and discussed less.

I believe it was the influence of the First World War that started the change from this pattern of individualism, and men who had joined the Army when assistant surgeons, and returned as seniors or soon-to-become seniors, began to break away from stale tradition. The two men in my own School

who were particularly progressive in a public-spirited sort of way, "keeping their eyes always on the heights", were Sir Leonard Parsons, our late Dean, and Seymour Barling, my teacher and predecessor. Without giving offence they broke down the rigid correspondence between firms: they urged and succeeded in establishing more beds for the assistant staff, and a more rapid advancement in status than the ordinary passage of time necessarily gave. They introduced the rule, and the necessary facilities for implementing it, that newly appointed members of Staff should study abroad for a year. They published much, including one of the most comprehensive textbooks on the diseases of children.

Similar changes were, of course, taking place in other Centres, for it was becoming recognized universally, even if grudgingly, that in order to make progress, young men must be given encouragement and means to develop some particular line of their own, as well as opportunity for travel.

But it is since the Second War that the general environment has so changed; indeed, things have moved at such a pace that we do well to ask ourselves whether in the right direction, and to what extent we have the power to modify it. I will not dwell on the Health Act, but I cannot refrain from saying that, so far as hospital work is concerned, never have I worked with better equipment, more assistants or such adequate laboratory facilities; never has it been easier to obtain new apparatus and instruments; and if a worthy project has been formulated by a group of the Staff, never has it had a better chance of early achievement. If anything, this adds to our responsibilities, for it is fundamentally important, urgent and essential that we should shake ourselves out of the spirit pervading the scene during our formative years, of make and mend, patch up or do nothing because of perpetual financial stringency, and, through our Medical Advisory Committee to the Board of Governors, and our medical representations on the Board, initiate all the improvements we can think of in every phase of hospital activity. That, I am sure, is what the lay members of the Board look for and expect, and wherein lie our continued influence and increasing authority even under the new authorities; but, if we do not make these contributions ourselves, it will be done by somebody else, and not always to our liking.

The Endowment Fund, handed back to teaching hospitals so that the interest may be spent on amenities to patients and on medical research and education, is treasure indeed, and, speaking for my own School, I can say that it has enabled us to embark on planned researches such as never before.

One difficulty of national planning is its tendency to create fixed patterns. For instance, the newer specialities which, after all, are the growing edges of surgery, have been designated before full experience has decided their definitive boundaries. Indeed, for a really alive speciality, boundaries are artificial, for in its amœba-like activities it will impinge and encroach on others, absorbing this, exchanging that and sometimes handing back something to general surgery. As an example, when the Ministry was discussing plans in the early stages of the Health Service, the surgery of the heart was in its earliest stages: to-day the demand for mitral valvotomy threatens to swamp the speciality, yet it is right and proper that this work should go to the thoracic surgeons. Should not some of the problems which their technique has improved come back to general surgery?

We must not allow the newer specialities to be isolated in small hospitals remote from others, as the Ministry was at first inclined to do; and the arrangement whereby, under one roof, preferably that of the teaching hospital, all are represented by token units, seems good, since it enables all to rub shoulders with one another and, at the same time, to keep in contact with the steadying influence of general surgery. Each exponent will then realize what he may not have done before—that he is not the only one who is making discoveries and advancing his subject. This presupposes a system of regular discussions. One of the things I admire most in America is their clinico-pathological conferences, seminars and grand rounds, and it was most noticeable that at any Centre you visited any member of Staff would know the mortality rates, five-year survival rates, numbers of this, that and the other types of disease admitted, for his particular hospital. To my mind, the conference habit is the life-blood of a progressive School, and I think that every candidate for Staff status should be informed that he is required to give at least one hour, and preferably more, each week to such meetings.

What are we going to do about the continued fragmentation of surgery that we are witnessing to-day? Certain it is that progress is made by the man who interests himself in some particular disease or group of cases and, thereby, adds to knowledge, and he may attract to himself so much of this type of work as to force him to give up all else, and thus a speciality is born. But unless it embraces a large volume of work, or demands special ancillary services as with fractures, or requires to be carried out at a different tempo as in neurosurgery, it should not be perpetuated as a speciality. If the man has done his job properly he should have passed on the fruits of his experience to younger men, and it should then return to general surgery. As Ernest Gask used to say, the knowledge of the specialist of to-day becomes the property of the general surgeon a decade hence. This, of course, is only partly true, but is another way of saying that there are no rigid boundaries. Dr. Churchill used to refer to the three generations of a speciality: the first consists of the pioneers, those who really discover, the men with a vision; the second, trained by the first, are the torch bearers, the experts, the finished article, so to speak; the third tends to become the mechanical, repetitive technician, without much verve or imagination; and besides, by this time, the limelight will be focused elsewhere. We must not let Whitehall planning make boundaries too rigid.

Another American feature I would much like to see introduced here concerns the training of surgeons, and it is fitting that it should be mentioned in the centenary year of Halsted who did so much in formulating a policy for the training of surgeons. One year of their six or seven years of training is spent in a laboratory of some kind, it may be anatomy, physiology, experimental surgery, or one of some more fundamental discipline, such as biology, biochemistry or even electronics. There he will learn to use a library, to assemble apparatus, to understand a scientific jargon, and will rub shoulders with others engaged in research, and listen to their discussions. He will acquire the habit of observing, measuring and experimenting in order to test his theories. During this year he loses nothing financially, nor in seniority, and, at the end of it, there is a job of appropriate responsibility awaiting him at the hospital. When I spoke of this to the Ministry they suggested that a man of ambition, wishing to spend a year in this profitable manner, should be prepared to accept a lower salary; but this misses the whole point, that it would only be to the exceptional man that such a year would be offered, and that it would be to the benefit of the Service to foster such men. We must convert the Ministry to support this plan, otherwise only bachelors and men with private means could afford to obtain the best education.

What of the scientific approach to surgery? Is it just fashion? When one thinks of recent advances, such as the new anæsthetic drugs and apparatus; the more accurate matching of blood groups and better preservation of blood banks; the newer sulphonamides and antibiotics; the better understanding of fluid, crystalloid and protein balance and how to recognize and correct imbalance; the contributions of experimental surgery to the surgery of the brain, blood vessels, heart, œsophagus and the use of transplants; one realizes that more and more the clinician is carrying out his own experiments, and that he needs laboratories adjacent to his wards. Not all surgeons will wish to do this, of course, nor will all have time, but communal facilities should be available, administered for general convenience and economy by those spending most time at the hospital. It is especially important for the young man to grow up in such an environment of constant enquiry and to be able to worry out a problem for himself. This enthusiasm for scientific research does not mean that I do not regard operative technique as of high importance. It has even been suggested that a straining after technical perfection is beneath the proper function of a teaching hospital and that it should more properly be left to the large non-teaching hospital. Personally, I should regard as a failure any school or whole-time unit that could not produce the very highest degree of operative skill which, of course, includes pre- and post-operative care, just as I should regard it as a failure if there was not complete faith in its clinical opinion and judgment. Nevertheless, a school that is not actively engaged in seeking new knowledge, and bringing up men in an environment of enquiry and experiment is little more than a technical college.

If then, it is possible to control our environment, what would one like to see in one's own hospital? I should like to work in a hospital where all specialities are represented by token units of sufficient size to accommodate a fair cross-section of the diseases dealt with by each, together with about 200 beds for general surgery. I should like to see the conference habit strongly developed, so that all members of Staff attend a clinico-pathological conference, under a rotating chairmanship, at least once a fortnight. In addition, there would be appropriate clinics, seminars and rounds for special subjects. I should like to see research laboratories near the wards with facilities for biochemistry, pathology and isotope work. Somewhere in the hospital would be communal workshops for making apparatus, and also a communal animal house and attached operating theatre. For teaching hospitals, there should be some individual, or some group, tactfully co-ordinating the whole, and planning and organizing the teaching of students. Whether it be a whole-time professorial unit or a director does not matter; it is a co-ordinator that is wanted. There should be a fund to make it possible to invite leaders from elsewhere to spend some weeks as Visiting Surgeon, an arrangement that is a great stimulus to the hosts. This fund should also help senior trainees and members of Staff to visit other Centres, especially abroad. Finally, I should like to see it possible for outstanding trainees to spend one year in a laboratory, not necessarily away from the wards, but free from clinical duties, and without loss of salary or seniority and with a promised job at the end of it.

Such a programme is not a dream; indeed it forms the environment of many Centres to-day.

Section of Neurology

President—MACDONALD CRITCHLEY, M.D., F.R.C.P.

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Tactile Thought, with Special Reference to the Blind

PRESIDENT'S ADDRESS

By MACDONALD CRITCHLEY, M.D., F.R.C.P.

RÉSUMÉ

A NUMBER of observations upon what might be termed the neurological aspects of braille reading may be cited:

(1) The empirical invention of braille typology stands very near the limit of normal tactile discriminative powers. Each symbol, and there are sixty-three of them, is made up of one or more bosses within a "cell" or cluster of six possible places. Only a few signs comprise one point: many are made up of 2, or 3, and some of 4 or 5 dots. Now 6 points happens to be the normal limit of the power of discriminating separate contacts at a single, synthetic, immobile contact. This takes place by a process of immediate subitizing of separate stimuli. Of course, if the exploring finger moves, synthetic touch becomes an analytic touch, and stimuli beyond the figure of 6 can slowly be appreciated. Louis Braille's empirical invention still further keeps within physiological capacities in that his embossed dots are set at a distance of either 2·5 mm. or 3·0 mm. apart: we remind ourselves that the minimum distance which constitutes the usual threshold of tactile discrimination over the pulp of the finger-tips is about 2·0 mm. Each symbol, therefore, stands always just within the bounds of human achievement; but when one recalls that, in reading a page of braille, the blind person is sensing and interpreting about 2,000 to 2,500 embossed points a minute, the degree of accomplishment can be appreciated.

(2) The practised braillist is able to read with his master finger, rapidly and accurately, up to maybe 100 words a minute. He can still do so, even if a cloth is interposed between his finger and the page: or, indeed, even if he wears gloves and then reads through an intervening piece of material. In many blind persons, the master finger is exclusively one-sided, though well-taught braillists should be able to read with either index finger. Even so, there is always a manual preference, the hand of choice reading faster than the other. In nearly three-quarters of bimanual braille readers, the left hand is the one preferred. Ordinarily, the left forefinger hurries ahead and reads half of one line, which is then completed by the right finger, the left finger having already dropped down to the start of the next line of print. In other braille readers, one forefinger, say the left, marks the beginning of each line, leaving the other forefinger to act as interpreter. Yet another technique is for the right forefinger to sweep briskly across the page, interpreting the easy symbols, leaving the left forefinger to follow and to help identify unusual collections of symbols, by means of swift small-range searching movements. In this case, the one finger is devoted to the "service of recognition", and the other to the "service of control".

(3) As the blind reader passes the finger-tips of his two hands over the page of braille type, it may often happen that actually the tips of several fingers simultaneously touch the punctographic symbols, but of these many finger-tips, only one is "attending to" the nature and meaning of the symbols. The sense data from the other fingers are neglected, or disregarded: with most blind readers, there are more cutaneous areas simultaneously stimulated than are essential for reading purposes (*see* Fig. 1).

(4) Although it has been said that the pulp of one or more fingers "learns" to read the meaning of braille symbols, the "learning" process, of course, does not reside in the finger-tips, but in the cortex. Or, in any event, it is transcortical. The physiological mechanism behind an acquired sensorimotor co-ordination of this sort is still debatable.

FIG. 1.—Attitude of a blind girl reading braille. The two index fingers are the only ones concerned with the actual identification of the symbols, and yet the other fingers of the right hand are in contact with the paper. The sense-data from these finger-tips are not "attended to" during the act of reading.

(5) Through practice, a skilled braillist ceases to pay attention to the constituent dots forming a punctographic cell: he identifies each symbol as a whole—a tactile Gestalt. This fact ties up with the question of the comparative legibility of the various braille signs. That some are easier to read than others is not surprising, but the principles determining legibility are still rather obscure (*see* Fig. 2).

(6) Sensory perception is largely an appreciation of a *change* of state. Hence, a moving stimulus is more readily appreciated than one which is stationary; and a stimulus which fluctuates in intensity is felt more keenly than one of uniform magnitude. The effect of a moving stimulus can be achieved by passing the palpatory organ over an immobile object.

(7) Braille reading is often said to be very tiring. Prolonged sessions lead to a generalized feeling of fatigue, but, in addition, it is said that the tactile sensibility of the finger-tip becomes reduced.

(8) Braille reading, and stereognosis applied to unaccustomed test-objects, bring up the question of manual preference in the act of palpation. Most blind persons, as already said, prefer to use one hand rather than another for braille reading, and this hand has little to do with the question of ordinary cerebral dominance. Similarly, in his efforts to identify a difficult test-object, the normal blind-folded subject may display a manual preference.

Tactile Imagery

Vision is biologically so important a special sense that even in those who lose their sight at a relatively early age, a visual type of thinking may continue, or at any rate, it may modify the kind of imagery. The blind person retains a visual frame of reference. Most blind persons

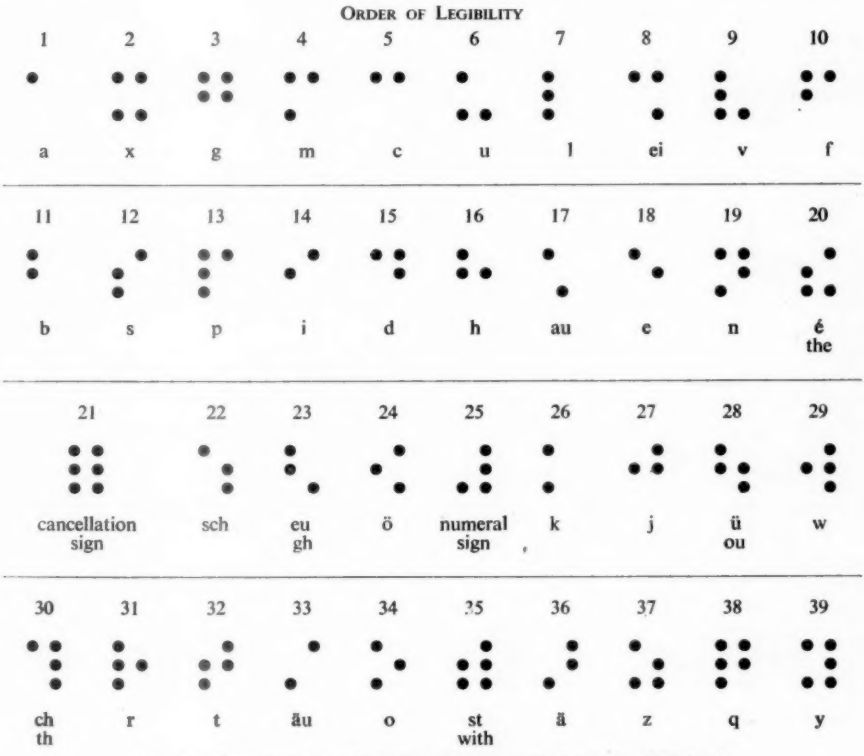

Fig. 2.—The comparative legibility of braille symbols. (After Bürklen.)

probably construct an "image of a visual image", even of faces, persons and scenes they have never had the opportunity of appreciating visually. To one who is blind, a particular person may be represented imaginally not only as a "voice", clothed in the bodily contours of which they may or may not have had tactual experience, but as a visual convention . . . a faint symbol which may bear but few resemblances to the original. Visualization is often quite vivid even though the patient may have been blinded early in life and thus have had a relatively short background of visual sense. Furthermore, visual experiences are not constantly being renewed, and yet these remote sensory experiences linger and continue to influence powerfully the nature of the imagery.

This explains why blind persons commonly speak of "seeing" a page of braille, or a person, or place, when they really mean "touching", "experiencing" or "feeling".

Many of the questions which concern imagery turn largely upon the duration of the blindness. Visual impressions are dominant in the realm of the senses and they are not easily forgotten. The shorter the history of blindness, or to put it another way, the later the age at which the subject lost his eyesight, the more established is the role of visual associations.

The importance of tactile thinking in the blind becomes obvious in so far as their body-image is concerned. The body-image of those born without sight must be quite unusual. This idea can be confirmed by a study of the graphic and plastic art of the blind, especially when the human form is depicted. Bodily parts which for the moment assume especial importance are generally exaggerated. The hands and fingers are often of excessive size, as mirroring the dominant part played by the organs of touch in the blind person's body-image.

Haptic Space

A psychological study of the blind confirms that tactile phenomena contribute to spatial perception and also to the subject's idea or notion of surrounding space. Révész made a distinction between "optohaptics" (which is the touch world of sighted individuals), and "pure haptics" as experienced by the blind. Blind persons are conscious of a space world which is smaller than in the case of those who can visually sweep the distant view and relate objects in the environment one with another, and with themselves. The blind cannot gain a knowledge of large objects, especially at a distance, for they need to pass their exploring hands over the contours of an object in a laborious fashion in order to be informed. Touch is, however, superior to vision in so far as the solid properties of small objects can be quickly realized by the examining hand. Villey has spoken of *manual* space, *brachial* space and *ambulatory* space, as making up the spatial notions of the blind. The first two are largely aspects of the body-image, and hence belong to the domain of personal space. The hands serve as linkages or outposts connecting personal with extrapersonal space. Beyond ambulatory space, which represents the range of a few paces only, lies the "touch horizon" which delimits remote space of which the blind person has but a hazy conception. For orientation within this remote space, he largely relies upon acoustic stimuli which, as they vary in intensity, may bring about considerable deceptions.

The blind are probably not deeply interested with abstract, mathematical or philosophical ideas of space, but rather with the simplest possible concrete geometric relationships between one tactually perceived external object and another. They are not much concerned with the ordinary cardinal directions within their haptic space, and for them a conception of accurate horizontal or vertical orientation is not important.

Particularly in the vertical dimension are the blind person's spatial ideas defective. Accurate conceptions of height are difficult for them, unless the object happens to lie within the range of their examining hand. Space is for them a much more compressed environment, for they cannot direct their gaze upon the surrounding panorama and divert their attention from one distant object to another. Things that they can hold and examine within the compass of their hand evoke a pseudo-visual image, but often a relatively small one. Larger objects which have to be felt by dint of wide angle arm movements give rise to a less vivid imagery, and here too the impression is one of smallness.

The spatial difficulties of a congenitally blind person include a number of notions which, being ordinarily pure visual phenomena, are not easy to achieve. For example, it requires a certain intellectual effort to understand what sighted people mean by perspective, and the notion can be taught only by way of a tactile analogy. The idea of a reflection in a mirror is yet another phenomenon almost as hard to explain to a blind person as that of colour.

Section of Urology

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Hydronephrosis

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CLASSIFICATION

HYDRONEPHROSIS may range from slight tubular dilatation to the replacement of the kidney by a vast hydrocele-like sac. The level of the obstruction may range from a kidney calyx to the bladder. A distended bladder, whether full of urine or even papillomata, is a powerful cause of ureteric obstruction and hydronephrosis. Obstructions below the bladder such as urethral stricture may give rise to hydronephrosis but mainly secondarily by producing a full bladder.

Various terms are applied to hydronephrosis. It is obvious that the condition may be unilateral or bilateral: the terms "open" and "closed" are used when urine does or does not escape from the sac.

Either renal or pelvic types of hydronephrosis may predominate but are most commonly found in some degree of association. Two factors determine which type will occur: firstly the lower the obstruction the more renal the hydronephrosis and, conversely, the higher the obstruction in the ureter the more pelvic the hydronephrosis.

Secondly the nature of the kidney itself: if the pelvis is intrarenal its capacity for enlargement is limited and a renal type of hydronephrosis results. With an extrarenal pelvis a "pelvic" type of hydronephrosis will be seen.

In many cases of lower urinary obstruction a sausage-shaped tumour results in which the transition from pelvis to the vast hydro-ureter is not definable.

Causes of hydronephrosis.—Male and female proportions are equal and there is no particular age incidence (Table I). It is sometimes familial. In endeavouring to arrive at some classification I prefer to classify congenital hydronephrosis first (Table II), and then to add acquired hydronephrosis afterwards. This has some surgical basis, as so often in the latter group the treatment is to be directed to the cause only.

Rare causes will be omitted to avoid confusion.

TABLE I.—ANALYSIS OF 200 CASES OF HYDRONEPHROSIS

	Incidence
Males	107
Females	93
Age 1–12 ..	30
13–30 ..	53
31–45 ..	60
over 45 ..	57
Bilateral	48
Right-sided ..	78 (2 solitary)
Left-sided ..	74 (3 solitary)

TABLE II.—CLASSIFICATION OF CAUSES OF CONGENITAL HYDRONEPHROSIS

Urethra	Epispadias
	Hypospadias
	Posterior urethral valves
Bladder	Deformity—extrophy
Ureter	Ureterocele
	Anomalies of number
	„ „ situation, e.g. retrocaval
	Valves
	Strictures
	Kinks
	Vascular obstruction
Pelvis	Abnormal insertion, form and number
Kidney	Abnormal situation

Acquired.—Obstruction affecting the urethra, bladder and ureter:
Lumen: Stone, foreign body, clot.
Wall: Neoplasm, cysts, inflammatory causes, fibrosis (infection, trauma + operation) spasm and hormonal causes affecting the wall, bladder diverticulum, neurological causes, prostatic obstruction.
Extramural: Neoplasm, fibrosis, any pelvic swelling.

Two hundred consecutive cases presenting as hydronephrosis have been analysed here (Table III).

TABLE III.—ANALYSIS OF 200 CASES OF HYDRONEPHROSIS

Cause	
1. Congenital anomaly of kidney	52
2. Acquired kidney disease	48
3. Ureteric lesion	29
4. Bladder lesion	19
5. Miscellaneous	9
6. Unstated but probably group 1	43
	200

This classification can obviously be extended but tends quickly to become unwieldy if that is done.

In double kidney the upper element is smaller. Only a few cases to the contrary have been reported (Ross, 1948). In reduplication of the ureters, the element from the upper kidney opens lower in the bladder, anywhere on a line from the ureteric ridge through the posterior urethra to the vulva and inner side of the thigh.

Two types of congenital hydronephrosis are worthy of special consideration.

(1) Congenital mega-ureter and hydro-ureter.

(2) Hydrocalicosis.

(1) Congenital hydro-ureter and mega-ureter do not include ureterocele, which is recognized as a ballooning of the terminal ureter associated with a meatal stenosis and weakness of Waldeyer's fibrous sheath often accompanied by vast dilatation of the ureter above.

Congenital hydro-ureter and mega-ureter are much more complex, and more difficult to understand. Some simplification is at once gained by recognizing two types: (i) A dilated ureter ending in a terminal narrow spindle; (ii) the dilatation persists to the bladder with a widely open orifice allowing reflux. Campbell (1948) refers to the former as hydro-ureter and the latter as megalo-ureter. The pathology is so different that two distinct terms are necessary to separate them and these appear the best at present:

Hydro-ureter with a terminal narrow spindle, as in hydronephrosis.

Megalo-ureter for the wholly dilated ureter and orifice; a rare condition.

From the time of G. Simon in 1871 a vast amount of writing has been done by various authors, but almost all on small series of cases only. Up to 1942 these have been reviewed and classified by Karl Østling in his book "The Genesis of Hydronephrosis", and the following explanations are offered by various authors:

(1) Valves; (2) twists and kinks; (3) fibrosis; (4) achalasia; (5) congenital defect in innervation (von Lichtenberg), and (6) congenital disturbance in growth causing dilatation. Østling himself investigated 250 fœtus and injected the ureters with liquid rubber and obtained ureteric casts. He demonstrated folds in the ureter (often spiral-shaped) as early as 5 cm. fœtus. He states that no urine was found and is not formed before parturition and that dilatations are not due to mechanical hindrance. Hydronephrosis and hydro-ureter in the fœtus are due to disturbance of normal growth. Persistent fœtal folds may cause hydronephrosis, as also may high insertion of the ureter.

To all this may be added fibrosis producing true strictures later and immense hypertrophy of the wall of the pelvis.

(2) Hydrocalicosis: This term was used by the late Kenneth Watkins in 1939 although isolated descriptions of the condition had appeared from the time of Rayer in 1841. Recently more light has been thrown on the subject by the paper read by Thomas Moore at the British Association of Urological Surgeons meeting in June 1950. He prefers the name hydrocalicosis, to the terms renal cyst, pyelogenous cyst and calyceal diverticulum, believing the condition to result from achalasia of the calyceal sphincters. The terms renal cyst, pyelogenous cyst, and calyceal diverticulum have all been used.

I personally can see no difference except in degree between these various conditions, but there is no doubt that chronic pyelonephritis can also produce and aggravate existing lesions of this sort.

Symptoms

It must be stressed first of all that a large number of cases are symptomless and may be discovered accidentally on clinical examination for some other reasons (e.g. life insurance and antenatal); while another large group of patients remain in apparently good health for many years until the supervention of some complication draws attention to the hydronephrosis.

(A) *Pain* is a prominent feature. 127 of 200 consecutive cases in Table IV presented with pain and only 66 were infected.

Table IV.—Analysis of 200 Cases of Hydronephrosis

Symptoms		
Pain	127	
Vomiting	33	
Hæmaturia	39	(The only symptom in 7)
Tumour	14	(„ „ „ „ 5)
Frequency	42	(„ „ „ „ 4)
Other	14	
Symptomless	3	
Infected	66	
Uninfected	134	

Pain is divided into three types:

(1) Pain due to distension of a hollow viscus. In the majority of cases the pain is extremely severe and is located posteriorly in the area between the 12th rib and the erector spinæ muscle, and anteriorly below the ribs. This may depend on the relative renal or pelvic nature of the hydronephrosis but in view of the usual combination of the two, pain is frequently felt both in front and behind.

During the attacks the ureter itself may go into severe spasm producing colicky pains along its course. This is sometimes confirmed at ureteric catheterization during an acute attack. The catheter is gripped by spasm and may bring on the ureteric pain before the hydronephrosis is reached.

The attacks of pain may occur spontaneously but in some patients there seem to be constant underlying features, e.g. some relate to a definite position in bed.

In a case reported by Covington and Reeser (1950) all attacks of pain were brought on by excessive ingestion of fluid. So genuine was this that an I.V.P. with restricted fluids was normal, while an I.V.P. with free fluids showed the hydronephrosis. This was an aberrant vessel type and suggests that in cases of doubt the I.V.P. might be repeated without fluid restriction.

(2) Pain may be due merely to the weight of the enlarged organ, and is described as a dragging pain with some radiation.

(3) Thirdly pain may be a result of the cause or of a complication. Stone provides a good example of both.

Referred pain must also be mentioned and is noted most commonly along the line of the ureter (although I think this is often true ureteric pain and not referred), and in the shoulder—omalgia. Contralateral renal pain and bowel pain are sometimes experienced.

(B) *Infection* is an important symptom, particularly in infancy. Meredith Campbell (1951) shows that out of 235 clinical cases of hydronephrosis in infancy 149 had pyuria and 93 had fever, while only 60 had pain.

So important is the underlying hydronephrosis that all cases of urinary infection in children should be investigated to exclude hydronephrosis.

In paraplegia, infection at once suggests the presence of urinary stagnation, whether in bladder or in a hydronephrotic sac.

(C) *Hæmaturia* is surprisingly rare as the only symptom (only 30 out of Campbell's 235 and only 7 in Table IV had symptomless hæmaturia).

(D) *Abdominal swelling* occurred in 15 of Campbell's cases and in 14 of my 200.

(E) *Gastro-intestinal* includes diarrhœa and vomiting from chronic uræmia.

Probably vomiting is associated with colic in some infants where the pain may be overlooked.

(F) *Various symptoms such as frequency, copious pallid urine, and even acute uræmia* must be mentioned to make the list complete.

(G) A most important group, however, is formed by symptoms produced by the cause or by

complications. Again ureteric stone is a good example, but infection must be stressed as a flare-up of this may lead to such severe symptoms of pyelitis or cystitis as to mask the underlying pathology. A few patients present with hypertension, urinary investigation revealing the hydronephrosis.

Complications.—The main complications of hydronephrosis, e.g. infection, stone, uræmia and hypertension, have been mentioned briefly under symptoms. All that remain to complete the list are occasional rarities.

There is undoubtedly a slightly greater tendency for a distended kidney to rupture at a blow and in two of such cases a vast pseudo-hydronephrosis developed and drained through the hole in the pelvis. I have met three cases of ruptured hydronephrosis.

Fistula may develop usually as a result of trauma, probably surgical, from a failed plastic operation and usually to the skin.

Investigations.—While obviously a urologist will tend to stress the importance of special investigations, in fact he does carry out a careful clinical examination, but this point should be stressed for the benefit of more junior surgeons.

The patient's general condition, fat or thin, wide or narrow costal margin, length of 11th or 12th ribs, will have a bearing on the choice of operation and its approach.

Merely talking to a patient may give some indication of the patient's capacity for co-operation in what may be a tedious and protracted form of treatment.

Variations in size of an abdominal mass may be noted to coincide with a change in symptoms. The fact that the kidney is palpable does not mean it is enlarged. It may be ptosed.

A palpable ureter whether *per abdomen*, *rectum* or *vaginam* is always pathological.

The blood pressure should be noted particularly with thought of the future.

Undoubtedly the first special examination is the intravenous pyelography which allows assessment of size, situation and function of both kidneys. It must be stressed that it is only the state of the kidneys at the time that is revealed. There is no measurement of renal reserve or of irreversible changes in the kidneys; these must be gauged from experience helped by a careful history and interpretation of the case.

In addition some indication of the cause of the hydronephrosis may be given; stone, aberrant vessel, ureterocele, &c. The importance of the preliminary film cannot be exaggerated.

Compression should not be used at all for the first set of pictures; clubbing of the calyces, stagnation in the ureter and a totally false impression may result. It is of great value, however, when further information is required and all such films should be clearly labelled "with compression" to avoid confusion. McLaughlin and Bowler (1952) stress the need for pictures in the erect position.

The main contra-indication to I.V.P. is uræmia—chiefly because it is a waste of time and also because of some possible increased risk to the patient. In cases of doubt, therefore, a blood urea test should precede the I.V.P.

Intramuscular pyelography is of help in tiny children and others where intravenous injection may be difficult. I first learnt about this in Stockholm in 1938 and have used it with benefit since that time. Special preparations are now made and hyaluronidase is advocated in allowing quicker absorption from the subcutaneous and intramuscular planes.

Aortography is not the terrifying project it was, and may be of help in planning plastic operations where information is required about a possibly abnormal vascular supply.

Presacral oxygen may assist I.V.P. in certain fat or gassy patients where definition is poor and difficulty experienced in ureteric catheterization for retrograde pyelography. The technique is simple and almost devoid of risk.

Cystoscopy will be found necessary in the majority of cases, but must always be undertaken with every possible precaution against infecting stagnant residual urine in bladder or kidney. An antibiotic cover is used for this investigation.

Cystoscopy is necessary (1) to obtain a catheter specimen for organisms and their sensitivities to the various antibiotics; (2) to measure bladder residual urine, e.g. in paraplegic cases; (3) to ensure a normal state of the urethra and prostate; (4) to exclude ureterocele and bladder diverticulum (particularly in cases with hydro-ureter); and (5) to allow ureteric catheterization and retrograde pyelography to be carried out.

Ureteric catheterization and retrograde pyelography are not without danger of infecting a perfectly sterile kidney. It is important not to make the patient worse with investigations. The indications for a retrograde may be briefly stated as follows: (1) Poor secretion at the I.V.P.; (2) to determine accurately the level of an obstruction; (3) to exclude various shadows from the line of the ureter. The value of oblique pictures cannot be sufficiently stressed, as well as the ten-minute withdrawal film.

The risk of infection by a ureteric catheter is so great that the following precautions are suggested:

(1) Careful technique.

(2) Antibiotic cover.

(3) The use of new ureteric catheters from a separate sterile container in hydronephrosis cases.

(4) Ureteric catheters used in infected cases to be thrown away. This is not an extravagance: a ureteric catheter is vastly cheaper than even a few extra days in hospital.

In certain patients the need for a retrograde pyelography can be avoided by a repeat I.V.P. with compression which will be considered a great advance, but nevertheless, the state of the urethra, bladder and urine may still require assessment by cystoscopy.

These investigations provide information about the kidney as it is; little guidance is available as to its capacity for recovery. I shall mention later the value of Pituitrin in the treatment of selected cases of hydronephrosis. I have now extended its use to their investigation.

Fig. 1 shows a bilateral hydronephrosis from a contracted tuberculous bladder which gave no view at all at cystoscopy.

After a course of Pituitrin (fresh) 0·5 c.c. daily for one week a new series of I.V.P. pictures were obtained (Fig. 2). Here the right kidney is now normal—the left is diseased and distended. The patient had a right uretero-colostomy and a left nephro-ureterectomy.

This Pituitrin investigation is worth carrying out in cases of hydronephrosis from either full or contracted bladders and in renal sympatheticotonus.

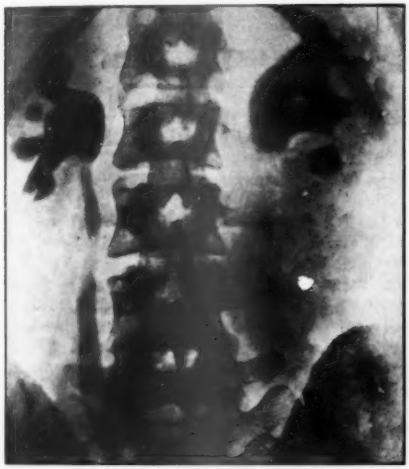

FIG. 1 (31.10.51).—Bilateral hydronephrosis in a case of contracted tuberculous bladder.

FIG. 2 (3.12.51).—After one week on Pituitrin. Normal right kidney. Left side unchanged.

The last point in investigation to be mentioned is that of patience. Many of these cases are not urgent from the pain aspect and the renal function may be deteriorating extremely slowly. In many cases of doubt as to the right approach to the case further intravenous pyelographies at quarterly or even yearly intervals may be recommended before the right programme is decided finally.

Differential diagnosis.—Urology is such an exact science that diagnosis should be exact. The only differentiation required is between the various types and degree of hydronephrosis to enable appropriate treatment to be carried out.

TREATMENT

The range of treatment for hydronephrosis is extremely wide. Nephrectomy, partial nephrectomy, nephropexy, nephrostomy, nephro-ureterectomy, uretero-neo-cystostomy, ureteric meatotomy, uretero-colostomy, renal sympathectomy, and plastic operations on the kidney (Table V). In addition, there is, of course, an equally wide range of treatments to the cause such as removal of stone, ureterectomy for carcinoma of ureter, and even prostatectomy.

TABLE V.—TREATMENT

Nephrectomy	79
Nephrostomy	10
Nephro-ureterectomy	6
Removal of renal stone	8
Plastic operation	8
Renal sympathectomy	5
Division of aberrant vessels	4
Transplantation of ureter:	
into bladder	2
into colon	2
Pituitrin	9

(1) *Medical treatment* by tradition must be considered first and consists mainly of no treatment. For example, recently admitted under my care, a man of 71 with acute retention from a large simple prostate was found to have no secretion from his left kidney due to a congenital hydronephrosis with an aberrant vessel. Prostatectomy was performed but no treatment recommended for the hydronephrosis apart from adequate antibiotic cover during the recovery from the operation. The condition was unilateral, symptomless and unlikely to start trouble after 71 years.

Medical treatment may be reserved for symptomless, unilateral cases in elderly people and for bilateral cases with only mild symptoms where the rate of deterioration is less than the expectation of life. Infection of a hydronephrosis provides one of the main indications for medical treatment; modern antibiotics (appropriate to the sensitivity of the causal organisms) are invaluable; one of the milder "sulpha" drugs may be used to maintain the sterility of the urine for a time.

In hydronephrosis of pregnancy such a routine usually serves to tide the patient over until after delivery; this treatment can be adopted when for other reasons the hydronephrosis is likely to be only temporary (e.g. a stone descending the ureter, or œdema of the ureteric orifice following cysto-diathermy for a papilloma). But infection is dangerous and can destroy a kidney quickly, so that if there is no quick response to antibiotics, the use of an indwelling ureteric catheter for a few days must be considered. Much stagnant urine can be drawn off, the position of the catheter checked by X-ray and continuous drainage established into a sterile receiver.

In the acutely infected stone case, if the catheter will not pass the stone, immediate operation must be carried out to remove the stone or even a temporary nephrostomy performed in more unfit cases.

I must refer again to Pituitrin. Lapides (1948), writing on the physiology of the ureter, shows that contraction of the human ureter is independent of the central nervous system and all its ganglia, and the only stimulus is the stretching of the smooth muscle by urine; that is, by diuresis. He states that Pitressin causes a decrease in urine excretion. However, Jona in 1928 showed that Pituitrin produced rhythmic contractions and I have used Pituitrin (which must be fresh) since his paper here in 1936.

Its value is undoubted in the hydronephrosis of paraplegia as I have shown in 1949 (Yates-Bell) and this has been strongly confirmed by Dr. L. Guttman (1949).

In fact I would now go further and say that part of the treatment of paraplegics is a regular intravenous pyelography so that if any incipient hydro-ureter or hydronephrosis is noted, a short course of Pituitrin (ten days with 0·5 c.c. daily) can be given. The benefit will only be transient if there is a systolic bladder or if a large residual urine is allowed to persist. There will be no benefit if fibrosis has occurred: this is found in longstanding hydro-ureter, particularly after attacks of infection. No benefit occurs with mechanical obstruction at the uretero-pelvic junction.

The indications for Pituitrin therapy are:

(*a*) Hydronephrosis with paraplegia.

(*b*) Early hydronephrosis with pain and spasm due to renal sympatheticotonus. A few cases are cured but owing to the underlying nervous instability of these patients many relapse and tend to respond less well to future courses of treatment.

(*c*) Transient obstruction of the lower ureter; good examples of this are patients who have a ureterocolostomy and experience renal pain.

(*d*) As an aid to diagnosis.

(2) *Treatment to the cause* must be of first importance and often is the only treatment needed. Examples—removal of stone from ureter, diverticulectomy.

(3) *Minor surgical procedure.*—I do not dilate ureteric strictures because I think if a catheter or bougie can be introduced there is no stricture. I agree that this is excessively dogmatic but I do believe that many non-existent strictures are so treated (perhaps with benefit for some other reason).

Ureteric meatotomy: endothermy is preferred. It is of very great value and may be all that is required in ureterocele. Ureteric catheterization has already been mentioned in the relief of colic and infection.

(4) *Nephrectomy.*—Nephrectomy for hydronephrosis had been accidentally performed several times before Gustave Simon made the first deliberate nephrectomy.

Nephrectomy has until recent years provided the most satisfactory treatment for unilateral disease. It is easy, safe (except in carcinoma, no nephrectomy had died in the Urological Department at King's College Hospital for twenty-five years). It has no remote complications such as urinary fistula, or the development of hypertension.

It still remains the ideal treatment for a unilateral hydronephrosis with little function.

(5) *Nephro-ureterectomy.*—A ureter which, if left behind, could cause stagnant secretions, infection, stone or pain must be removed. It can, of course, be done at one operation with the nephrectomy or if circumstances justify in two stages.

(6) *Uretero-hemi-nephrectomy* is sometimes carried out where a double kidney exists and one element is afflicted by hydronephrosis and hydro-ureter. I have done this as a bilateral procedure on a girl of 6 years.

(7) *Partial nephrectomy* is of use in hydronephrosis mainly when this is localized to the upper or lower pole as in hydrocalicosis, often associated with stone. For its successful outcome nature must have arranged the vascular supply to suit the operation which in fact is usually the case. Stewart (1950)

reports 71 cases of partial nephrectomy. Yunck and Forsythe (1941) report 19 cases of calyceal resection.

(8) *Nephropexy* is now rarely used by itself but it is the custom of many to fix the kidney at the conclusion of some other procedure such as division of an aberrant vessel or a plastic operation.

(9) *Nephrostomy.*—This is needed as a temporary measure to drain a kidney which may be obstructed or infected.

The operation is readily performed through a short incision designed to lie away from any expected subsequent incision and the tube is introduced through the convex margin of the lower pole of the kidney. Two tubes may be used if renal irrigation is likely to be required for any reason.

Nephrostomy is often used as an accompaniment of plastic procedures but is becoming less necessary and less popular for this purpose.

As a permanent measure it is unfortunately sometimes the only way of keeping alive a patient with advanced bilateral hydronephrosis, or with hydronephrosis of a solitary kidney; in the past it has proved necessary for persistent urinary fistula after failure of a plastic operation.

(10) *Renal sympathectomy* may be tried for hydronephrosis due to sympatheticotonus to relieve pain and to prevent deterioration. Usually these patients will have responded at first to Pituitrin but have relapsed sufficiently severely to demand treatment. Relief from the operation is immediate but results are disappointing as the symptoms tend to appear elsewhere, in the opposite kidney, in either ureter, in the bowel or even as Raynaud's disease.

(11) *Uretero-neo-cystostomy.* This, perhaps the most unsatisfactory of all operations for hydronephrosis, is necessary for a stricture of the terminal ureter such as results from a cystodiathermy, radium or other operative trauma; results for this are fairly good. Unfortunately it is required more often for hydro-ureter (with the narrow terminal spindle) and for the narrow junction of a double ureter.

The best that can be promised to a patient is better drainage of the hydro-ureter with less likelihood of deterioration and infection.

(12) Diversion of urine by *uretero-colostomy*, cutaneous ureterostomy or even cystotomy may be necessary for hydronephrosis resulting from systolic bladder or from chronic retention. Tuberculosis, Hunner's ulcer and certain nerve bladders provide these cases and great relief is obtained although with a high operative risk. Time is not available for further discussion of this valuable treatment.

(13) *Plastic operations on the pelvis and ureter.*—From 1891 when Küster (1896–1902) reported a reimplantation of a ureter into the pelvis, an enormous variety of operations has been devised to conserve the kidney. Fenger's longitudinal incision sewn up transversely, Albarran's orthopædic resection and many others produced a variety of operations with a variety of success.

1921 saw von Lichtenberg's paper. The principle of lateral anastomosis between ureter and pelvis combined with the splinting with a ureteric catheter and nephrostomy drainage has been employed by many surgeons until recent years.

Personally I have not been happy with the results. I have had too many failures of the union resulting in urinary fistula, poor drainage leading to infection and even the apparently successful case has needed urgent nephrectomy later for hypertension. The result was that I performed plastic operations only when absolutely necessary, preferring nephrectomy where possible as it seemed to me that many plastic operations ended as nephrectomies anyway.

The multiplicity of modifications confirms the dissatisfaction felt by most. The Cumming tube for nephrostomy, a sort of de Pezzer catheter with a proboscis to splint the ureter. Splinting of end-to-end anastomosis with a T tube (Deming, 1951). Gibson (1945) gives the history of all this.

Two main principles become established. Firstly lateral anastomosis of ureter to pelvis and of ureter to ureter superseded end to end (Gjessing, 1951; and Sayegh, 1952). Secondly ureteric splinting was adopted in most cases. Davis (1943) allows a narrow ureter to regenerate around the splinting tube and maintains that therefore the lumen of the new ureter will equal the size of the tube (he uses a size 14 gall-bladder tube). Now, however, with further advances, these procedures may be reserved for purely ureteric lesions.

Hamilton Stewart (1947) for lower polar artery obstruction aims at returning the kidney to its fœtal shape by bringing together the upper and lower poles of the kidney and sometimes plicating the pelvis. I have no experience of this operation but consider that it certainly deserves a place in kidney plastic surgery for aberrant artery cases.

On the whole if the aberrant vessel were small I would prefer to divide it and if it were large to embark on what we may now call an Anderson plastic (Anderson, 1949).

Winsbury-White (1950) suggests that if too large an aberrant artery be divided, a lower pole partial nephrectomy must be considered.

Anderson plastic.—This carefully planned but simple operation has at last given me great hope in plastic surgery of the kidney. The strictured ureter and redundant pelvis are excised, the lateral anastomosis between ureter and pelvis is so devised that drainage is truly dependent and with the least risk of stricture.

No nephrostomy or splinting tubes are necessary, so that with modern chemotherapy and antibiotics the course is usually afebrile, while leak of urine is kept to a minimum by careful suturing.

A powerful urinary acidifier should be given after all plastic operations on the kidney to prevent the deposit of phosphates.

Conclusion

Our knowledge of the pathology of hydronephrosis has greatly increased with consequent benefit to the patient.

Investigations should now lead to an accurate diagnosis in all cases.

As yet there is little to be done for gross hydronephrosis in newborn infants with prenatal renal damage; but, apart from this, antibiotics and improvement in the wide range of operations now available (particularly the Anderson plastic) are of such importance that the disease may be arrested with the patient in comfort. Death should not now occur from hydronephrosis.

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The following cases and specimens were shown:

(1) **Giant Bilateral Hydronephrosis.** (2) **Sarcoma of Penis.**—Mr. Hugo Grant.

Renal Aneurysm.—Mr. Alex. E. Roche.

(1) **Carcinoma of Kidney in Child of 12 Years. ? Bournville Syndrome.** (2) **Papilloma on a Ureteric Valve.**—Mr. R. A. Mogg.

Ureteric Obstruction (Two Cases).—Mr. R. Helsby (for Professor Charles Wells).

Bacterial Calculus.—Mr. Charles Dundon (for Mr. Harland Rees).

Chronic Abscess of Urachus.—Mr. C. I. Murphie (introduced by Mr. S. Power).

(1) **Carcinoma in Vesical Diverticulum.** (2) **Urethral Diverticulum.**—Mr. Thomas Moore.

(1) **Urethral Diverticulum.** (2) **Priapism Due to Leukæmia.**—Mr. T. L. Chapman.

Leukæmic Ulceration of the Penis.—Dr. D. E. Sharvill (introduced by Mr. J. G. Yates-Bell).

Tuberculous Prostatitis Complicated by Perineal Fistulæ.—Mr. S. G. Tuffill.

Gumma of the Epididymis.—Mr. Harland Rees.

Section of Endocrinology

President—S. LEONARD SIMPSON, M.A., M.D., F.R.C.P.

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Pituitary-Adrenal Hyperfunction

PRESIDENT'S ADDRESS

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ABSTRACT

(1) Nearly all endocrinology is genetically determined, familial and so-called constitutional, and there is no sharp dividing line between endocrinopathies and accepted normality. The main points of endocrine instability are puberty, pregnancy and the climacteric.

(2) The adrenarche may extend over a number of years before and after the menarche and involves both adrenal androgens and adrenal glucocorticoids.

(3) Various hormones augment appetite, producing "metabolic appetite in the midst of plenty" and may also change the percentage proportions of body fat or protein.

(4) Adrenal hyperplasia may progress to adenomata and ultimately to a single adenocarcinoma, with subsequent involution of the other adenomata. This may also be true of pituitary basophil, or eosinophil, hyperplasia.

HORMONE ASSAYS IN ADIPOSE GYNISM AND GYNANDRISM

I HAVE previously reported (Simpson, 1951) Bornstein's assays by hepatic glycogen method in 5 of my patients with adipose gynism, urinary values being 50% or more above adult female values. Mr. Reginald Gardner, working in Dr. W. W. Payne's Laboratory at The Hospital for Sick Children, Great Ormond Street, has undertaken an investigation of a larger series of patients with adipose gynism and gynandrism, using a copper reduction-arseno-molybdate method (modification of Talbot *et al.*, 1945), and expressing the result as water-soluble partition fraction. His results support Bornstein's biological assays, again comparing with adult values, and are given below in detail (Table I). Normal children's urinary values appear to be lower but as the numbers of controls were smaller, I have used adult values for comparison. This also tends to obviate the measurement per kilogram or per square metre potential modification. It is true that I have chosen the more severe examples of my syndrome and that milder examples may give normal values. Also one patient, weighing 37 st., and initially giving raised values, subsequently on a low calorie diet gave normal values, suggesting an influence of diet on adrenal function, possibly in both directions. The 17-ketosteroids appear to be normal or raised but show much variation.

TABLE I.—HORMONE ASSAYS—URINE

Reducing glucocorticoids partition fraction—Normal range adults=0·6 to 1·4 mg. per 24 hours.
Normal range children 12 to 15 years=0·3 to 0·8 mg. per 24 hours.

Initials	Age	17-ketosteroids per day	Volume urine ml.	11-oxysteroids per day
Adipose gynism:				
A. C.	13	9·9	1,500	4·8
J. F.	8	6·27	1,495	2·84
K. H.	13	5·7	950	2·8
E. B.	15	12·2	1,600	2·06
M. L.	14	6·2	820	2·87
A. L.	11	4·08	610	2·3
V. N.	12	5·2	1,160	2·4
S. O.	8	4·8	600	2·51
D. T.	10	4·1	750	1·8
M. W.	15	8·1	520	3·92
B. C.	20	17·3	2,746	4·07
Adipose gynandrism:				
B. F.	13	13·4	1,920	2·30
C. P.	10½	3·6	670	1·8
D. S.	12	6·75	1,000	2·5
C. J.	18	14·1	960	6·0

Five of my patients with adipose gynism have also been investigated by the paper chromatographic method of hormone assays in urine, permitting the assay of different fractions (Bush, 1951*a*). Constance de Courcy and Barbara Lunnon, working in Professor C. H. Gray's laboratory, have given me the following brief interim indication of the trend of their results:

"We have examined the urines of 5 patients with adipose gynism and compared them as a group with a group of 10 normal females. The mean value for the excretion of Compound E in adipose gynism is 30% higher than that of normal females. The increase in Compound F is about fourfold. Other adrenal cortical metabolites, probably biologically inactive, occur in two to three times the amount found in normal female urine.

This statement is limited by the fact that the comparison has been made between normal adult females and girls aged 10 to 13."

Plasma ACTH.—Delphine Parrott (1951) has carried out assays on 5 of my adipose gynism patients; 4 showing raised values, comparable to those found in Cushing's syndrome, namely 214, 242, 177 and 171 micrograms ACTH per 100 ml. plasma compared with the normal range of 60 to 110; and the fifth giving a raised value of 208 initially but a normal value of 71 six months later with some clinical amelioration.

A summary is given below of 5 out of 24 cases of pituitary-adrenal hyperfunction of whom photographs were shown:

Case I.—Gigantism with acromegaly and familial adiposity. J. O., female, aged 13½. Referred by Dr. Victoria Smallpeice. Height 78 in., weight 230 lb. Normal till age 4, then grew rapidly and developed deep strong voice; at 12 developed pubic hair. Age 13 adipose, red lineæ on abdomen and back, nose and lips enlarged, acne; shoes size 12½ (adult), enlarged big toe; thick greasy hair; no thyroid enlargement; no menstruation; optic atrophy; 17-ketosteroids 9·6 mg.; corticosteroids 3·4 mg. Parents average size, but the girl had a paternal aunt 76 in. tall and very fat, and a great-uncle, a blacksmith, tall and exceptionally strong and weighing 560 lb.

Case II.—Adrenogenital virilism. V. G., female, aged 36. Menstruation normal 14 to 16, when amenorrhœa developed together with hirsutism, deepening of voice and increase in weight. Big-boned woman with prognathism. At age 21, radiography after Uroselectan showed right adrenal tumour, which was removed by Mr. Muir Dickson. Menstruation became regular again but hirsutism persisted. The 17-ketosteroids were very high before operation (143 mg. per day), and although reduced by more than 50% still remain very high (55 mg. per day as compared with the normal of 5 to 12 mg.). Abdominal laparotomy eleven years after operation did not reveal any neoplasm in the pelvis or adrenal areas; the left adrenal was moderately enlarged. Hirsutism still persists. A primary and persistent pituitary stimulus is postulated.

	1938	4 mths. after operation	18 mths. after operation	1952 14 yrs. after operation
Carbohydrate tolerance	90, 142, 166, 160, 156 mg.			
17-ketosteroids ..	135 mg.	60 mg.	—	35 mg.; 55 mg.
Œstrogens ..	200–400 M.U.	100–200 M.U.		
Gonadotrophins ..	5,000 R.U.	250 R.U.	< 25 R.U.	Aschheim-Zondek negative
11-oxysteroids ..				4·0 mg. crude; 2·5 mg. water soluble
Plasma ACTH				285 units (normal 60–110)

Case III.—Cushing's syndrome—bilateral adrenalectomy (Fig. 1). L. S., female, aged 23. Referred by Dr. R. Byron Evans, Cardiff. Average baby and child; menarche at 14, became fat. At 21, adiposity increased; amenorrhœa. At 23, gross adiposity; severe pain lumbar spine; severe osteoporosis; compression fractures; cyanotic facies; broad purple lineæ distensæ on chest, abdomen, flanks and thighs; scalp hair thin, dry, brittle.

28.1.52: Seven-eighths right adrenal removed (Professor C. G. Rob, St. Mary's Hospital). 10.4.52: Left adrenal gland removed (Professor Rob); cortisone therapy twelve days. 26.5.52: Discharged feeling well; face less red, obesity decreasing. 6.8.52: Readmitted for routine investigations. Skin and bodily contours show great improvement; feels very well; first menstrual period for 2½ years. September 1952: Well; no substitution therapy required. Considered to be normal.

Assay results:	Before operation	After operation
17-ketosteroids ..	13·3 mg.	0·5 mg. 1·4 mg.
11-oxysteroids ..	3·7 mg.	1·3 mg. 1·7 mg.
Sedimentation rate	24 mm.	8 mm.

Case IV.—Cushing's syndrome—bilateral adrenalectomy. A. B., male, aged 39. Referred by Dr. Joan Walker. Normal childhood; highly coloured from puberty; very hirsute from age 17; polycythæmia age 20; athletic and strong as youth. December 1951: complained of tingling forearms, legs, mouth; polyneuritis; diplopia in evenings; glycosuria two months previously. Fat plethoric face with cyanotic tinge; scalp hair greasy with frontal retraction; fundi normal; no diplopia; hirsute whole body and limbs; limbs thin; marked lordosis; prominent abdomen; violet lineæ lower abdomen; extensive osteoporosis and compression fracture D.11. Carbohydrate tolerance 213, 327, 408, 411, 294; sedimentation rate 22 mm.; cholesterol 200 mg./100 ml.; 17-ketosteroids 12 mg.; glucocorticoids (water soluble) 5·7 mg.; leucocytes 8,600; polys. 87, lymphos. 11, monos. 2%.

11.2.52: Seven-eighths right adrenal gland removed by Professor C. G. Rob, St. Mary's Hospital.

24.3.52: Left adrenal removed completely (Professor Rob). Somewhat stormy recovery; weakness and pyrexia; maintained on daily doses cortisone (25 mg., later 12·5 mg.) and salt.

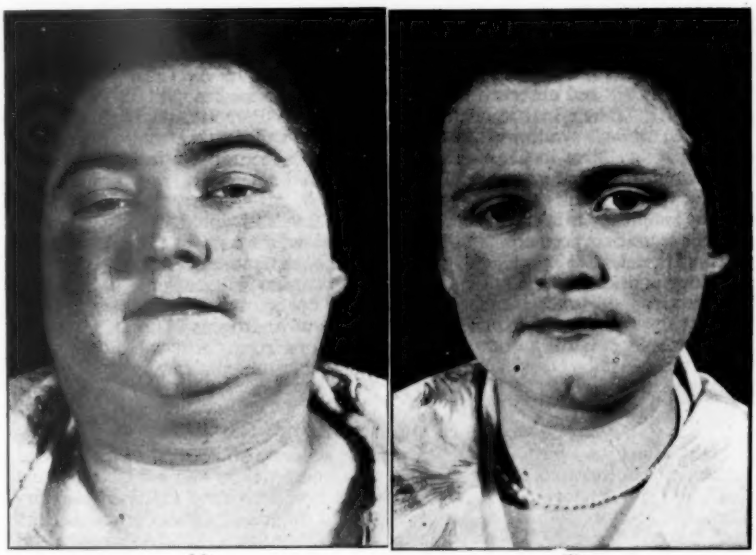
May 1952: Carbohydrate tolerance 92, 154, 231, 170, 145; sedimentation rate 7 mm.; cholesterol 153 mg.; 17-ketosteroids 4·6 mg.; glucocorticoids (water soluble) 3·9 mg. (under cortisone); leucocytes 9,000, polys. 55, lymphos. 37, monos. 2; eosinos. 6%.

August 1952: 17-ketosteroids 6·8 mg.; glucocorticoids 0·67 mg. Main features of Cushing's syndrome disappeared but weak and rapid pulse.

September 1952: sedimentation rate 9 mm./1 hr.; 17-ketosteroids 5·6 mg. ACTH tests showed chronic adrenal insufficiency. Improved on 25 mg. cortisone daily.

Case V.—Cushing's syndrome with pituitary tumour. E. B., female, aged 35. Always fat child; menarche age 13, oligomenorrhœa 1–4 months. Age 20, amenorrhœa, adiposity, plethora, hirsutism, red lineæ. Age 21, Cushing's syndrome diagnosed; X-ray revealed intrasellar tumour, rarefied dorsum sellæ. Age 23, Married. Four months later, after ? rubella, spontaneous disappearance of all symptoms. Age 26 male child born. Oligomenorrhœa but otherwise normal. Age 32, complete relapse to condition as at 20 following attack of measles. Sudden severe pain in lumbar spine, profuse growth hair on upper lip, cheeks and chin, axillary and pubic hair of male distribution, breasts atrophic and flat, extreme osteoporosis and collapsed vertebræ. B.P. 180/100; polyuria, polydipsia.

Height 62 in., weight 140 lb.; 17-ketosteroids 33·6 mg.; glucocorticoids 3·4 mg. (normal 1–2); glycogen steroids 136 μg. (normal 32–57); Hb 115, W.B.C. 10,000, polys. 78, lymphos. 15, monos. 7%; cholesterol 270 mg. per 100 ml.; phosphatase 23 (normal 3–10); plasma ACTH 305 μg. (normal 50–120); E.S.R. 4 mm.; specific gravity urine 1010; urea clearance 40%; carbohydrate tolerance normal. Irradiation of the pituitary fossa has had no beneficial effect and removal of the intrasellar tumour is contemplated.



(*a*) (*b*)

FIG. 1.—*Case III.* Cushing's syndrome treated by subtotal bilateral adrenalectomy (Prof. C. G. Rob). (*a*) Before operation. (*b*) Five months after second operation. (Photographs by Dr. P. N. Cardew, St. Mary's Hospital.)

PITUITARY SOURCE OF ACTH

In both acromegaly and Cushing's syndrome, there is enlargement and (or) hyperfunction of the adrenal glands, and the recent work of Delphine Parrott (1952) has shown increased plasma ACTH in both conditions. In the former, the pituitary hyperactivity is clearly located in the eosinophil cells, whereas in the latter the pituitary basophil cells appeared to be responsible. If so, it might follow that the eosinophil cells secrete a type of ACTH that increases adrenal androgens and the basophil cells a type of ACTH that increases adrenal glucocorticoids. The issue is not so simple. A woman of 40 (McCormick *et al.*, 1951) had a mixture of acromegaly and Cushing's syndrome, with the raised plasma ACTH reduced to normal by removal of an eosinophil adenoma. Many acromegalics without obvious adiposity show a moderate elevation of urinary corticosteroids. Further, Crooke's hyaline basophil cells, which were regarded by some as the source of ACTH, have now been produced in animals and man by injection of ACTH or cortisone (Golden *et al.*, 1950; Laqueur, 1951), and would therefore appear to be secondary to an excess of endogenous cortisone in Cushing's syndrome. If so, what is the cellular source of the excess of ACTH in Cushing's syndrome, or what other stimulus can cause adrenal hyperfunction? Cushing's original suggestion of a basophil adenoma has been excluded by its inconstancy, yet in one case (Cohen and Dible, 1936), a basophil carcinoma was the cause. There are a few cases of Cushing's syndrome in the literature with a grossly enlarged sella turcica and in Case V, a woman of 35, the large sella has been known to be present for some twelve years, as well as the Cushing's syndrome which underwent spontaneous remission for many years

before it returned with acute severity, and a very great increase of ACTH was found in the plasma. (It is incidentally difficult to imagine this ACTH to be the same type as that found in my case of the big-boned woman with hirsutism (Case II).) The existence of such cases of Cushing's syndrome certainly favours the pituitary origin of the disease (cf. acromegaly with and without enlarged sella turcica) but they do not necessarily exclude an abnormal responsiveness of the adrenals or cases due to a primary idiopathic adrenal neoplasm. The pituitary histological problems remain to be unravelled. The hypothalamic release of the pituitary ACTH stimulus under certain conditions is accepted (Bush, 1951*b*).

Heinbecker's production of Cushing's syndrome in dogs by hypothalamic lesions was associated with a preponderance of pituitary eosinophil cells, degranulation of the basophils and later hyalinization (Crooke cells) (Heinbecker, 1946). Severinghaus and Thompson (1939) injected dogs with sheep's pituitary extracts and produced Crooke's hyaline basophil cells. Moehlig and Bates (1933) found a marked preponderance of basophil cells twenty-four hours after adrenalectomy in 8 out of 11 dogs. Crooke and Russell (1935) studied the pituitary in 12 cases of Addison's disease and found some decrease in eosinophil cells, a much greater decrease in basophil cells, but the presence of many transitional basophil cells and an increase in the chromophobe cells. Laqueur (1951) found the hypertrophied non-granulated cells in adrenal insufficiency could be identified as basophil cells with the periodic acid Schiff technique, and he interpreted them as cytological evidence of increased ACTH-secreting function. In contrast, the hyaline basophil changes of Crooke were interpreted as decreased ACTH function and this must be true if they can be produced by ACTH injections (or cortisone). These recent experiments and observations tend to incriminate the basophil cells in relation to ACTH and corticosteroids. Taken in conjunction with Delphine Parrott's demonstration of increased plasma ACTH in Cushing's syndrome, the evidence appears sufficiently strong to restore the pituitary gland as the motivating force in Cushing's syndrome; with the non-hyaline granular or transitional basophil cells as a probable source of ACTH, with basophil adenomas (which rarely show Crooke's changes) and the rare basophil carcinoma as expressions of basophil hyperplasia, and the co-existent Crooke's cells as secondary to high corticosteroid plasma levels. I would also hazard a conjecture that the basophil cells secrete corticosteroid-producing ACTH and the eosinophil cells androgen-producing ACTH, granting that I have speculated beyond established facts and within the complex field of pituitary histology and its potentially dynamic cell interchangeability.

Although injections of testosterone reduce adrenal corticosteroids in urine (via inhibition of pituitary ACTH) and reciprocally, cortisone reduces adrenal androgens in urine by the same pituitary mechanism, yet atrophy of the opposite adrenal in the case of adrenal corticosteroid tumours (Cushing's syndrome) and the rarity of atrophy in adrenal androgenic tumours (virilism) tend to support the theory of two types of ACTH.

Is ACTH a Single Hormone? Further Considerations

Experimentalists have also postulated that there are at least two ACTH hormones, one indication being the absence of correlation between assays by adrenal weight and by ascorbic acid depletion. Thus Stack-Dunne and Young (1951) state: "We are now convinced that two pituitary factors at least are involved." Prunty and colleagues (1951) found the urinary glucocorticoids (formaldehydogenic) a much better guide to ACTH response than 17-ketosteroids. Shadaksharappa and colleagues (1951) reported that in myxœdema both the glucocorticoids (formaldehydogenic 0·5 mg.) and the 17-ketosteroids (1·7 mg.) were very low, whereas in human thyrotoxicosis the 17-ketosteroids were low (4·0 mg.) but the glucocorticoids raised (formaldehydogenic 3·0 mg.). They do not interpret their findings, but it would appear possible that this is a dissociation of adrenal cortex hormone secretions via two types of pituitary ACTH influenced, or determined, by thyroid function. Incidentally cortisone may cause a depression of thyroid function as measured by radioactive iodine, basal metabolism and serum protein-bound iodine (reviewed by Kuhl and Ziff, 1952). ACTH is closely related to pituitary melanophore expanding hormone and although it can be chemically separated (Morris, 1952), Sulman (1952) claims that in human endocrinopathies their quantitative assays run parallel.

With adrenal hyperfunction endocrinopathies in man, even in the absence of neoplasm, there would certainly appear to be an absence of consistency in the proportion of adrenal androgens and adrenal glucocorticoids found in the urine, sometimes the one or the other markedly preponderating. Such proportion determines the manifestations of an adrenal endocrinopathy as well as normal physical characteristics. We must either postulate endocrine glands of different innate responsiveness, or structure, or ACTH stimuli of different biological character. Such changes may be variable and dynamic. What starts them off or determines their character? What causes the initial pituitary stimulus, or stimuli, to the menarche or adrenarche, and how does it come about when it does? Pituitary-adrenal changes brought about by pregnancy or the climacteric are not too difficult to understand, but why does a pituitary-adrenal androgen mechanism become more intense say at the age of 35, or why does a child embarrassingly hirsute until the age of 7 suddenly become fat and lose the hirsutism or, biologically speaking, change from an adrenal androgenic excess to a glucocorticoid one? Why do some of my adipose gynandrism patients lose their fat at 17 and simultaneously become hirsute while others remain hairless, even with normal 17-ketosteroids, and become even more fat

in the next decade or so, and later develop hypertension and diabetes, the former type eating at least as much as the latter? Why do some adipose gynism patients become normal and others get worse with the years? What is the spring that determines the change of pituitary-adrenal mechanism?

Hyperinsulinism as a Factor in Adiposity

We will start with experimental hypothalamic adiposity, which is usually quoted to support the "gluttonists" or "mechanists" because a localized hypothalamic lesion produces voracious appetite and does so in the presence or absence of the pituitary gland. No one has yet found out whether this mechanism functions also in the absence of the adrenals, and Kennedy (1951) has recently shown that the adrenals are grossly enlarged in such rats. Apart from this, such hypothalamic-lesion rats outgain normal rats in weight increase even when paired fed, and gain weight on a diet which was only sufficient to maintain normal weight before operation (Brobeck, 1946). Respiratory quotient studies (Tepperman *et al.*, 1943) showed that the R.Q. in hypothalamic-lesion rats increased to well above unity when fed, and to a far greater degree than during glucose feeding to normal control rats, indicating a conversion of carbohydrate to fat at "a tremendously accelerated rate" (Brobeck, 1946) and they suggested that large amounts of endogenous insulin were necessary for the conversion. Incidentally pathological kidney changes were observed.

Ogilvie (1945), of Edinburgh, treated 15 rabbits with a crude ox anterior pituitary extract on a fixed diet which previously just maintained body weight. They increased in weight, even those who ate less through malaise. The pancreatic islets of the treated animals were twice the weight of the controls. Balmain, French and Folley (1950) refer to the work of Bloch and Kramer (1948), who used acetate labelled with ^{14}carbon to show fat synthesis; and themselves using slices of mammary tissue taken at the height of lactation, found that crystalline insulin produced respiratory quotients as high as 2, indicating its role as a regulator of fatty acid synthesis from carbohydrate and acetate.

Young (1951) found that growth hormone could increase the weight of dogs, continuing on a diet that previously could just maintain their weight, and that the addition of insulin caused the deposition of fat as well as protein. In answer to the question "Does pure growth hormone cause an increased rate of insulin secretion?" he gives a probable positive answer. Marx, Herring and Evans (1944) injected purified growth hormone into hypophysectomized rats which had been fasted for approximately eighteen hours. Within one to three hours, typical hypoglycæmic symptoms were observed, and the blood sugar level of these animals was invariably depressed further than that of untreated controls fasted for the same period.

Can Adrenal Hyperplasia Become Neoplasia?

I first considered the possibility in connexion with my unusual Case II, a girl of 21 with big long bones and prognathism, enlarged clitoris, extensive hirsutism, amenorrhœa, and excretion of 17-ketosteroids of 140 mg. per day. Removal of an adrenal adenocarcinoma restored menstruation but did not influence hirsutism, and the 17-ketosteroids remained high at values between 35 and 55 mg. per twenty-four hours. Laparotomy twelve years later showed no metastases but enlargement of the opposite adrenal gland, suggesting that a pituitary ACTH stimulus was still operating.

I similarly interpreted cases of sexual precocity in boys, e.g. Lynch (1950), in which removal of an adrenal tumour at 6 still left the 17-ketosteroids above normal (although reduced) and the adult facial and sexual hair persistent or augmenting. The presence of multiple adrenal adenomatous nodules in Cushing's disease in children (e.g. Chute *et al.*, 1949) and in some cases of acromegaly is also suggestive.

Harrison and Abelson's case (1952) of a girl, developing Cushing's syndrome at 11, undergoing laparotomy at 15, with the adrenals apparently normal, and then dying at the age of 30 with an adrenal carcinoma and pulmonary metastases, appears to point in the same direction.

It is well known that fœtal adrenal hyperplasia may produce sexual precocity in a brother and pseudohermaphroditism in a sister, but in one such case (Hain, 1947) the brother had an adrenal tumour on one side, which was not removed at operation, and which showed no signs of metastasizing five years later.

There is a certain amount of experimental evidence to support the thesis of adenomatous hyperplasia and subsequent malignancy. Thus Woolley (1950) found that in certain strains of mice, bilateral ovariectomy led to nodular hyperplasia of the adrenals, with nodules bulging through the cortex, and later the development of an adrenal cortical carcinoma which could be transplanted. This phenomenon was associated with the development of basophil tumours of the pituitary and with Crooke's hyaline changes. Adrenal and pituitary tumours could be prevented by stilbœstrol or testosterone but not by progesterone or deoxycortone. In the discussion following Woolley's paper, Hertz stated that castration followed by massive doses of œstrogens led to benign nodular hyperplasia in the adrenals of rats, with resulting enormous adrenals, one weighing 345 mg. Spiegel (1939) found that in guinea-pigs castrated at birth the penis continued to grow and the adrenals showed cortical adenomata.

If comparison with the thyroid is justified, Goldberg and Chaikoff (1952) induced thyroid carcinoma, with metastases, in rats (7 out of 25) with radioactive iodine ^{131}I, but could not produce malignancy with thyrotrophic hormone. Of 125 rats receiving thyrotrophic hormone for two years, 24 developed adenomata, some having thyroids fifty times the weight of the controls. Griesbach, Kennedy and

Purves (1945), with thiourea (rape seeds) in rats, produced uniform hyperplasia and then multiple adenomata of the thyroid; and Purves and Griesbach (1947), in similar experiments in rats, found that the adenomata could become malignant with metastases in the lung. Herrmann (1951) recorded 2 patients with toxic diffuse goitre receiving methyl thiouracil for three years, the woman of 54 years of age developing adenomata and the man of 69, adenocarcinoma. Sir Thomas Dunhill (1931) regarded hyperplasia, adenoma and adenocarcinoma of the thyroid in man as different phases of a transitional process and not distinct entities. I would conclude the same for the adrenal gland, while recognizing the possibility of an additional innate neoplastic responsiveness to an endogenous ACTH stimulus.

Note on Blood Sedimentation Rate

I have observed that the blood sedimentation rate is often raised in Cushing's syndrome, sometimes appreciably, and that after bilateral adrenalectomy it may become normal. On the other hand, and perhaps paradoxically, I have observed that the blood sedimentation rate is often raised in Addison's disease, regardless of whether the lesion is tuberculous or atrophic (idiopathic necrosis) as shown by subsequent autopsy; and further that while this raised sedimentation is uninfluenced by deoxycortone, it tends to become normal with cortisone therapy. This phenomenon does not depend upon the co-existence of any obvious infection. It is suggested from these preliminary observations that the level of blood corticosteroids has an important influence on sedimentation rate, possibly by influencing the composition or balance of blood proteins; but a larger series of cases must determine the consistency of the above findings.

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Clinical Section

President—HAROLD EDWARDS, C.B.E., M.S.

[*October* 10, 1952]

Behcet's Disease.—S. B. KARANI, M.R.C.P.

L. S., male, aged 24. Enlisted in the Army in 1947 (medical category A.1). In 1947 whilst serving in Egypt contracted bacillary dysentery and a few weeks after discharge from hospital noticed that both eyes became bloodshot and painful and the vision was blurred. The attack subsided in about two weeks, but recurred in a fortnight and these relapses have continued, affecting either one, or both, eyes, ever since. In May 1948, whilst on demobilization leave, he developed the first attack of erythema nodosum-like rash on legs and these attacks have also continued to recur at odd intervals. From August to November 1948 he had treatment at the Moorfields Eye Hospital for recurrent bilateral iridocyclitis. Since January 1950 the patient has also suffered from recurrent painful ulcers in the mouth (Fig. 1). In June 1951, when I saw him for the first time, he had an ulcer on his scrotum, which gradually cleared and never recurred.

This patient has therefore suffered from recurrent attacks of iridocyclitis, erythema nodosum-like rash on his legs, and ulcers in the mouth (Fig. 1) since contracting dysentery in 1947, and these relapses occur in any combination. So far, his general health has remained unaffected although each attack now makes him feel more languid. Repeated clinical examinations have failed to reveal any abnormal physical signs.

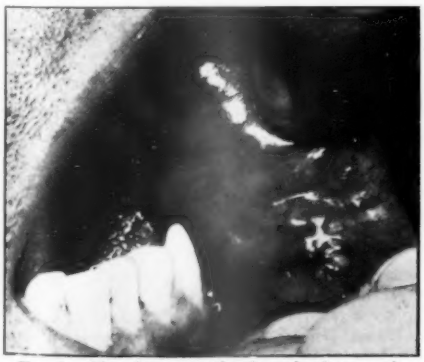

FIG. 1.—Showing necrotic ulcers in the mouth.

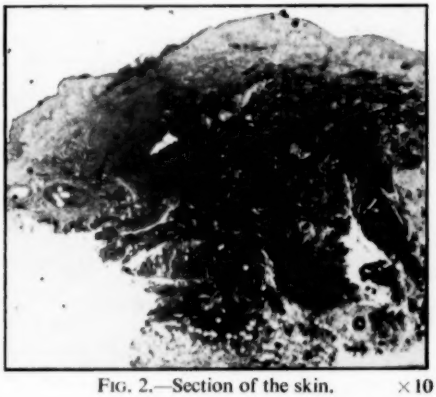

FIG. 2.—Section of the skin. ×10

Investigations.—X-ray chest and sinuses, sigmoidoscopy, urine and fæces, nothing abnormal revealed. Blood count, normal (hæmoglobin 90%), E.S.R. (Wintrobe) 30 to 40 mm. in the first hour. Serum proteins normal. Blood W.R., Kahn and gonococcal fixation test negative.

Herpes neutralization test (Colindale Laboratory): Antibody to herpes simplex present.

Mantoux test (June 1951): 1 : 1,000 strongly positive.

Skin biopsy from leg lesion (Dr. H. Haber): Fig. 2, a specimen submitted, demonstrates a marked allergic reaction lying within the lower cutis and subcutis. It consists of a marked proliferation and obliteration with thrombosis of vessels with fibrinoid degeneration of perivascular collagen in some places. There is also a marked extravasation, polymorphic infiltrations with leucoclasia demonstrable. The upper cutis shows an inflammatory reaction of subacute type.

In addition to simple antiseptic mouth-washes and antihistamine tablets, the patient has had antibiotics, vitamins, cortisone (locally for eyes) and ACTH without appreciable effect. Two months ago the patient's wife developed an attack of oral ulcers, which gradually cleared and has not recurred.

Comment.—Behcet's disease is a relatively rare chronic illness affecting primarily the uveal tract, the buccal mucosa, and the genitalia, but other parts of the body such as skin, joints, and the central nervous system are frequently involved. Since Behcet (1937) described the disease, about 33 cases have appeared in the literature and several authors have expressed the view that the disease perhaps has a common ætiology with Reiter's disease, Stevenson-Johnson disease and erythema multiforme. France *et al.* (1951) have stressed the following points:

(i) The disease runs a chronic course for years and the most dreaded complication is progressive loss of visual acuity. Either a complete remission or a fatal outcome is exceptional and the two deaths reported in the literature presumably resulted from involvement of the vital centres of the brain. One of these was a Yemenite from Palestine and the other a R.A.F. airman, who developed the disease whilst serving in Egypt. Histopathological sections reported by Berlin (1944) on the former case showed a non-specific round-cell infiltration in the meninges and the brain, micro-infarcts in the substantia nigra, perivascular round-cell infiltrates about the central retinal artery and in the choroid, and round-cell infiltrates in the liver and kidneys. The oral and genital ulcers showed non-specific inflammatory changes with fibrino-leucocytic exudate. Thrombosed blood vessels in the corium were found in sections from genital ulcers. So far as I can determine, this is the only post-mortem report available in the literature.

(ii) Biopsy studies suggest that the smaller veins may be a site of the basic lesion but the exact cause of phlebitis, which may either be inflammatory or allergic, or due to virus infection, and its peculiar distribution remains a mystery.

(iii) To date, no specific treatment has been found either to abort an attack or prevent a relapse.

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Dr. T. A. Kemp said that the only case he had seen had had thrombophlebitis migrans and was totally blind from retinal thromboses. He had ulcers in the mouth and round the scrotum.

Dr. Kemp thought that the name of R. L. Sutton had been attached to the disease.

Dr. T. Parkinson: In view of the widespread thrombosis noted in the biopsy material it might be worth trying the effect of prolonged therapy with anticoagulant drugs.

POSTSCRIPT (December 1952).—This patient has now had a full course of anticoagulant and estosterone therapy without beneficial effect.—S. K.

Œdema Due to Subacute Nephritis Treated with Ion-exchange Resins.—E. LAWSON MCDONALD, M.D., M.R.C.P., and K. N. V. PALMER, M.D., M.R.C.P. (for Professor A. KEKWICK, F.R.C.P.)

J. R., female, aged 39, was admitted to the Middlesex Hospital under the care of Professor Kekwick on November 9, 1951. She gave a history of increasing swelling of the legs during the preceding five weeks; this had spread to the lower abdomen, but did not involve the face. The onset of the swellings was sudden. There was no history of sore throat or hæmaturia. She had not been given any drugs known to affect the kidney.

She had suffered from asthma since childhood. This had been worse since the start of her present illness.

Family history.—Non-contributory.

On examination.—Gross pitting œdema of legs and lower half of the trunk, also of the arms. Mucosæ rather pale. B.P. 150/105. There were scattered rhonchi in the chest. Otherwise no significant abnormality was found. C.V.S.: Pulse regular, rate 104. Jugular venous pressure normal. Heart not enlarged clinically. No murmurs.

Special investigations.—Urine: Gross albuminuria.
Catheter specimen of urine: Scanty R.B.C. and leucocytes. No casts. Culture sterile.
Blood urea 37 mg./100 ml., although one week later it was 134 mg./100 ml.
Plasma: Total protein 4·5, albumin 1·8, globulin 2·3, fibrinogen 0·4 gramme/100 ml.
Serum cholesterol 643 mg./100 ml.
X-ray chest: Chest showed small bilateral pleural effusions.

J. R. ♀ AGED 39

A CASE OF OEDEMA DUE TO SUBACUTE NEPHRITIS
TREATED WITH ION EXCHANGE RESINS

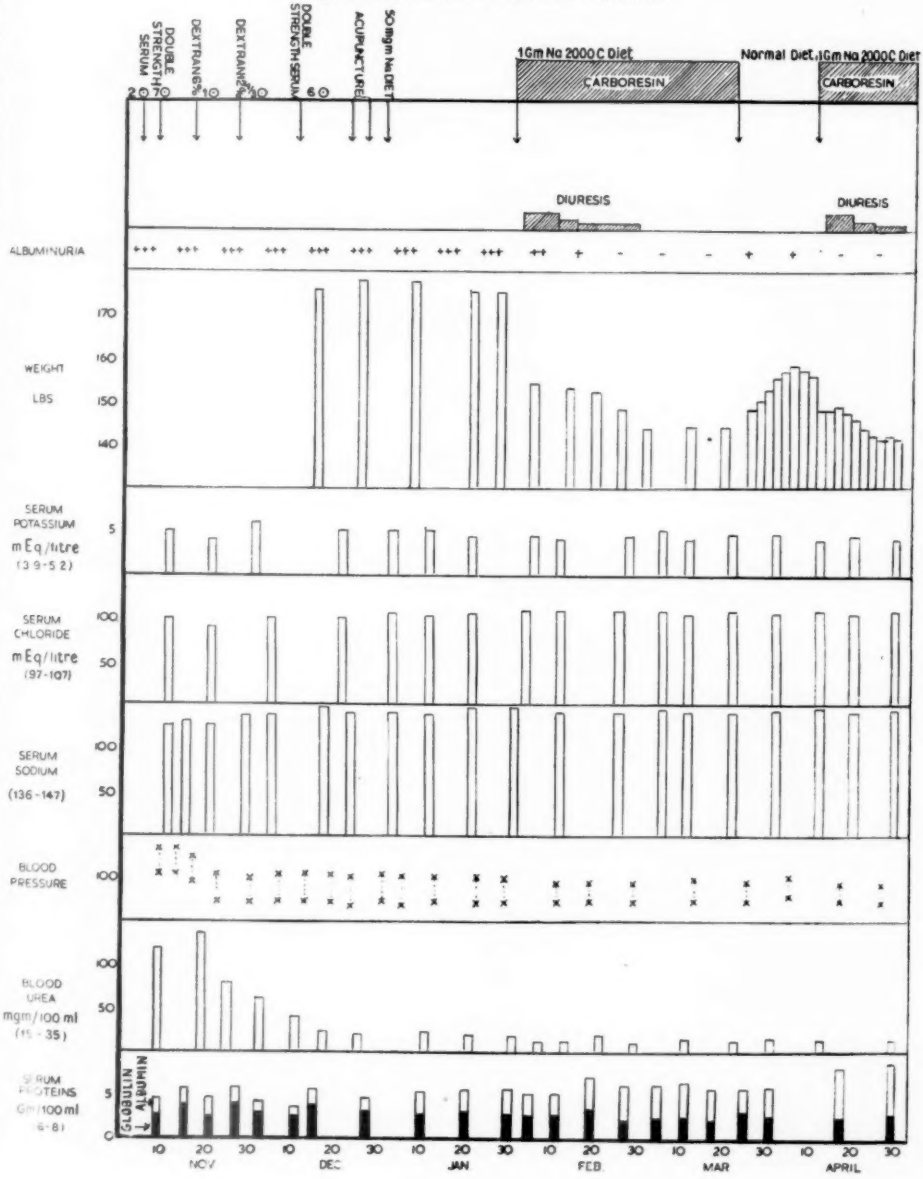

FIG. 1.

Progress (*see* Fig. 1).—During the first twelve weeks of her admission to hospital her condition improved in that the blood urea and blood pressure fell, but the œdema persisted and distressed her greatly in spite of rest in bed, Casilan by mouth, intravenous injections of concentrated plasma and dextran, a 50 mg. sodium diet and drainage of her œdema with Southey's tubes. About three months after her admission to hospital she was placed on a 2,000 calorie diet containing 1 gramme of sodium in twenty-four hours and given 16 grammes of carbo-resin three times a day. Carbo-resin is a mixture of a weakly acidic carboxylic acid cation exchange resin and a weakly basic polyamineformaldehyde anion exchange resin. One-third of it is present in the form of the potassium salt of carboxylic acid resin and two-thirds in the hydrogen cycle.

Within a few days the patient showed marked clinical improvement. There was a diuresis, she lost her œdema and there was a dramatic fall in her weight. Her albuminuria disappeared. On cessation of the resin and the resumption of normal diet on 26.3.52 the patient immediately gained weight and the albuminuria returned. When the previous diet and carbo-resin were resumed there was a diuresis with weight loss and her subsequent progress was satisfactory.

She continued on the diet and resin for four months. After this the dose of resin was gradually decreased and the amount of sodium in the diet increased. When seen on 9.9.52 she had returned to work, and volunteered that she had never felt better. She was on a normal diet. Clinical examination showed no abnormality and there was no albuminuria. The special investigations were within normal limits.

Comment.—The diuresis with marked weight loss which occurred in this patient coincided with the taking of carbo-resin by mouth. Previously the œdema was not reduced by several forms of treatment including severe sodium restriction, and appeared to be stationary. The disappearance of the albuminuria during the resin therapy and its return during the period when the resin was omitted is not readily explained. Its ultimate disappearance could have occurred in the natural history of the disease.

Summary.—An ion-exchange resin proved useful in the relief of renal œdema in a patient who had failed to respond to other measures.

Pregnancy Complicated by Mitral Stenosis and Pulmonary Tuberculosis Treated by Mitral Valvotomy.—T. PARKINSON, M.D.

Mrs. M. U., aged 25. No history of rheumatic fever or chorea.

1940 (aged 13): Cardiac murmur found on routine examination. No symptoms. 1943: Several hæmoptyses. Chest radiographs said to be normal. About this time she noticed slight dyspnœa on strenuous exertion. 1948: Further hæmoptysis. Radiography showed right upper lobe tuberculosis and the sputum contained tubercle bacilli. After a period of bed rest the sputum became negative and has remained so. Progress satisfactory until August 1952 when she reported that she was two months pregnant. There had been slight increase in dyspnœa during the last few weeks.

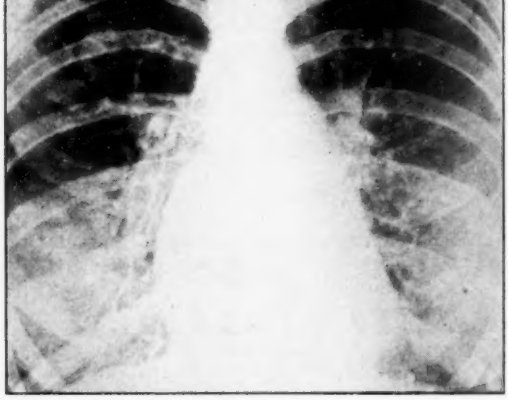

FIG. 1.—Radiograph of chest.

FIG. 2.—Tomogram of right upper zone.

On examination.—Classical signs of pure mitral stenosis were found, but there were no signs of congestive failure.

Investigations.—Radiography: Enlargement of pulmonary conus, a "round focus" in the right upper zone, infiltration at the right apex, haziness in the mid-zones (probably due to hæmosiderosis) and calcification in the lower zones (Fig. 1). Screening: Little enlargement of the left auricle. Tomograms: Confirm presence of a round focus in the right upper zone and show no evidence of cavitation (Fig. 2). Vital capacity: 1,950 c.c.

Circulation time (arm-tongue) 22 sec. ECG: Right ventricular preponderance.

Operation (16.9.52).—Mitral valvotomy (Mr. I. M. Hill). Pulmonary hæmosiderosis was confirmed during the operation. Recovery from operation was uneventful.

Comment.—Mitral stenosis and pulmonary tuberculosis were found together in this patient when she was nine weeks pregnant. The problems of treatment are of current interest since they must be considered in the light of surgical treatment of mitral stenosis. Clinically the patient had pure mitral stenosis; it had been present for twelve years and there had been no subsequent attacks of rheumatism; the left auricle was only slightly enlarged; there was a clear history that breathlessness was beginning to increase. The tuberculous disease had been present for four years. The history and radiological features indicated that there was a "round focus" in the right upper zone, or, more correctly, that the lesion was a tuberculous cavity, the bronchus of which was blocked. In the absence of other disease the safest treatment would have been surgical removal of the affected lobe, but this was hardly feasible in a patient with grossly diminished respiratory reserve. Treatment by bed rest or by termination of the pregnancy would only have deferred decisions about active treatment so it was decided that the best treatment was to do a valvotomy early in pregnancy and to allow the pregnancy to proceed to full term. Subsequent treatment of the tuberculosis will depend on the degree of recovery of pulmonary function after valvotomy. There has already been some improvement in symptoms and in the arm-tongue circulation time after operation. A disturbing feature was that Aschoff nodes were found in the biopsy material of the auricular appendage taken at operation. Extra difficulties must be anticipated in view of the frequent adverse effects of pregnancy on active rheumatic heart disease.

I wish to thank Dr. J. B. Shaw and Mr. G. C. Brentnall, who referred this patient to me, and Mr. I. M. Hill who carried out the mitral valvotomy.

Mr. N. R. Barrett: Dr. Parkinson has presented an interesting and difficult problem, namely, how to treat three separate conditions: pregnancy, mitral stenosis and pulmonary tuberculosis occurring in the same patient. I believe the line he has taken is wise and correct, but I would criticize his observations on two points:

I think he has conveyed the impression that the surgery of mitral stenosis has entered upon a phase in which it can be relied upon to produce good results. My own view is that this outlook is too optimistic, although I do not deny that many patients who would otherwise have died, or at best been crippled for life, have been returned to useful and active existence. But I do stress that the diagnosis as between mitral obstruction and mitral incompetence is not yet perfect. The surgeon who operates expecting to find stenosis and actually meets incompetence may not be well placed to treat his patient. Moreover, despite the enormous ability of the heart to work relatively efficiently in the face of gross anatomical and pathological abnormalities, it is a fact that the surgery of mitral stenosis to date merely alleviates a permanent structural abnormality.

For these reasons too much should not be expected until long follow-up has proved the lasting value of the operations at present performed on the mitral valve. In my own view these operations are crude and are the beginning of a new era. They will ultimately be replaced, if the demand persists, by accurate surgery.

My second criticism of Dr. Parkinson's observations is that, in our experience at St. Thomas's Hospital, at least a third of all patients operated upon for mitral stenosis have active Aschoff nodules in the myocardium.

Von Recklinghausen's Disease—Abdominal Tumour.—M. JOSEPH, M.B. (for REX LAWRIE, M.S.).

F. D., girl aged 11.

Past history.—When aged 18 months patient tended to stand only on heels. Diagnosed at hospital as mild poliomyelitis and plaster applied to left foot and leg above knee. Kept in plaster six months and began to walk a month or two after plaster had been removed.

At age of 5 years there was (*a*) 1 in. shortening of right leg and a calcaneus deformity of left with weak tendo achillis; (*b*) sacral spina bifida; (*c*) sacral pigmentation and hirsutism; (*d*) swelling of left vulva. The right shoe was raised ½ in. and she was given remedial exercises and faradism to left calf muscles.

At age of 8 years she was investigated for nocturnal enuresis but no organic cause could be found.

Present history.—(1) Pain lower umbilical region, present for about one year, occurs at irregular intervals, few days to few weeks. Lasts from a few minutes to an hour. No relation to food. Not severe and described as an ache, but did have one severe attack. (2) Frequency for some years $\frac{\text{D } 6\text{–}8.}{\text{N } 1\text{–}2}$ Difficulty in controlling micturition on leaning forward. (3) Pigmentation present since age of 9 months. (4) Hirsutism lumbar region.

Physical signs.—Skin: Café-au-lait patch lower abdomen and upper thighs. Reddened, thickened tender patches both buttocks with underlying mobile tender nodules (Fig. 1). Left vulva reddened, thickened and larger than the right.

Abdomen: Solid, mobile, nodular, irregular firm swelling, measuring 6 × 3 in., rising out of pelvis. The uterus could not be felt separately from the mass which appeared to lie well forward (Fig. 2).

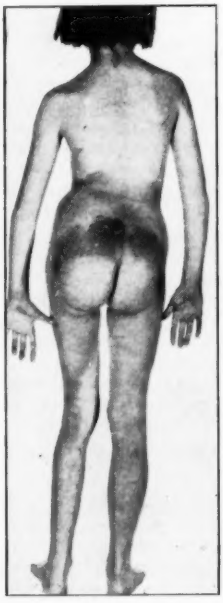

FIG. 1.

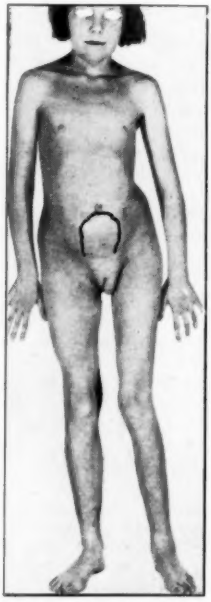

FIG. 2.

FIG. 1.—Shows lengthening and wasting of left lower limb, pigmentation of lower trunk and hairy patches of thickened skin on buttocks.

FIG. 2.—Shows outline of abdominal tumour and enlargement of left vulva.

Hips and lower limbs: Left side of pelvis tilted upwards. True lengthening of left thigh (1½–2 in.). Legs same length. Calves—1½ in. wasting on left. Abduction of left hip limited.

X-rays: Left femur is slender and there is some coxa valga which accounts for the lengthening.

Excretion pyelogram shows left hydronephrosis and hydro-ureter with an irregular deformity of the top of the bladder.

Operation findings (17.10.52).—Lower paramedian incision revealed that the lump consisted of a mass of neurofibromatous tissue involving almost the whole of the wall of the bladder. Removal was not attempted. No other lesions were found in the abdomen.

Malnutrition Due to Jejuno-colic Anastomosis.—IAN C. GILLILAND, M.D., M.R.C.P. (for M. R. EWING, F.R.C.S.)

T. S., aged 50. Electrician.

Past history.—Lupus vulgaris successfully treated by ultraviolet light in adolescence.

1918: Was operated upon for mass in right iliac fossa and a hemicolectomy performed. No further details available. "Swollen abdomen" for one year. Remained well until:

1932–47: Several admissions to hospital for acute obstructive episodes, treated conservatively except on three occasions when adhesions were divided.

1947: After further episode of small bowel obstruction, a stricture was found at the distal end of the small intestine. An ileo-colostomy was performed. Remained well and working until 1950. Weight at that time was 12 st.

1950: Left work because of a persistent cough and has not yet returned.

1951: In the six months prior to his admission, a quick and progressive deterioration had set in and he became virtually bedridden. He developed abdominal fullness with attacks of griping pain mainly in the right lower quadrant. He passed one large, bulky, offensive, pale stool daily. He had frequent vomiting and lost his appetite completely. He suffered from weakness and breathlessness and his weight fell to 6 st. 10 lb.

1951: He was admitted to Hammersmith Hospital 20.10.51 with subacute obstruction. Examination showed an emaciated, sunken, pale man with healed lupus of cheek and nostrils. There was slight brown pigmentation of the face and hands contrasting with the marked pallor of the mucous membranes. His blood pressure was 110/60 and there was slight pitting œdema of the ankles. He had a distended, tympanitic abdomen with multiple scars; this was tender mostly on the right side. Bowel movements were both seen and heard.

Investigation.—Stools bulky, pale and offensive. Three-day fat balance studies: 69% absorption; 82–80% nitrogen absorption. Hb 5 grammes%. R.B.C. 1,300,000. Reticulocytes 4%; mean corpuscular volume 143 cu.μ; mean corpuscular hæmoglobin concentration 39%; W.B.C. 3,000; 72% polymorphs.

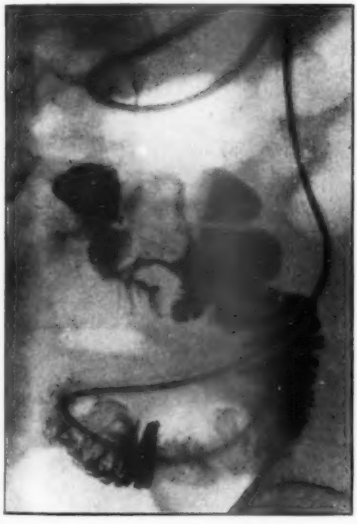

FIG. 1.—Miller-Abbott tube in position. Barium entering large intestine.

Sternal marrow showed gross megaloblastic change with accumulation of primitive cells. Free acid present in stomach.

Blood chemistry: Albumin 3·4, globulin 2·6 grammes%. Na 329, K 20, urea 40, calcium 8·1, P 3·9 mg.%. Bicarb. 48·1 vol. %. Urine Sulkovitch test negative. Creatinine 945 mg., creatine 362 mg./24 hours. Kepler test at the time was positive, the factor being 23. X-ray of chest showed old scarring at right apex. X-ray of pelvis showed ? generalized thinning and bilateral acetabular protrusion of osteomalacia.

Barium examination of the small bowel was carried out through a Miller-Abbott tube. 40 c.c. of barium were passed which then appeared simultaneously in a jejunal loop and in the transverse colon. No barium was seen to reach the lower jejunum or ileum and all passed into the colon (Fig. 1).

Pre-operative treatment.—He was placed on intragastric feeds supplemented with vitamins and B_{12} intramuscularly. He was given a course of streptomycin and PAS and DOCA 5 mg. daily for one week. After three months his general condition was greatly improved. His hæmoglobin was now 13·9 grammes %, his maximum reticulocytic response being 12% and he was considered fit for operation.

Operation (Mr. Ewing): A right hemicolectomy had been performed and also a jejunal-transverse colostomy about 4 ft. down the small bowel. Below this another 5 ft. of normal small bowel was encountered and then another 2 ft. showing 3 annular strictures.

The jejuno-transverse colostomy was undone, the continuity of the bowel restored, the strictures excised and a new anastomosis performed between the lowest part of healthy bowel and the colon in the region of the hepatic flexure.

Pathology.—Constricted area: Local mucosa is heavily infiltrated with eosinophils. The submucosa shows scarring, the muscularis is intact and the serosa shows local fibrous thickening.
Intervening area: Numerous eosinophils in mucosa.

Post-operative.—His post-operative course was marred in the first instance by a flare-up of bronchitis but there has since been steady improvement. Six months after the operation a barium meal showed: "Stomach mobile orthotonic with normal mucosa and peristalsis. Duodenal bulb regularly outlined. Small bowel pattern normal and no flocculation of barium seen. Rate of onward movement of barium was not abnormal and after four and a half hours the colon was outlined." His motions are coloured but still soft. Three-day fat balance: 94·3% absorption. Hb 15·6 grammes%. R.B.C. 4,900,000. Reticulocytes less than 1%. Mean corpuscular volume 100 cu.μ. Mean corpuscular hæmoglobin concentration 32%. Na 140 mEq/l K 4·5 mEq/l. Chlorides 106 mg.%. Urea 14 mg.%. Albumin 4·6, globulin 3·0 grammes%. Ca 10 mg.%. P 3·7 mg.%. Alkaline phosphatase 12 King-Armstrong units.

He is now walking about but complains of vague pains in lumbar region and lower spine. Weight 8 st. X-ray still shows osteoporosis.

Parathyroid Adenoma with Generalized Osteitis Fibrosa Cystica.—MARY C. HOLT, M.D., M.R.C.P. (for J. W. LITCHFIELD, F.R.C.P.).

B. F., housewife, aged 48.

History.—For three months prior to her first attendance at hospital on 8.4.52 the patient had been subject to widespread skeletal pain, particularly severe in the lumbar spine on sneezing or bending, and in the left foot when walking. During the same period she had also been troubled by lethargy, anorexia, and constipation, but there had never been any disturbance of micturition.

On examination.—Forward flexion of the lumbar spine was limited by pain. No other abnormality was found, and in particular no mass was palpable in the neck.

Investigation.—The discovery of a large area of bone destruction, with clearly defined edges, occupying the greater part of the body of the second lumbar vertebra (Fig. 1), led to the patient's admission to hospital two days after her outpatient visit. Subsequent X-rays revealed similar osteolytic lesions in the left fibula, the proximal phalanx of the left big toe, the parietal region of the skull, and the horizontal ramus of the left mandible in the vicinity of the molar teeth. The radiological picture was perhaps more suggestive of multiple myelomatosis than osteitis fibrosa cystica but the serum calcium level of 19 mg.%, with normal plasma proteins, strongly favoured the latter diagnosis. An electrocardiogram showed changes consistent with hypercalcæmia, and the latter probably also accounted for the persistent vomiting which developed after admission. The alkaline phosphatase was 21 units and the urine Sulkovitch test strongly positive. There was no evidence of metastatic calcification, but both urea concentration test and intravenous pyelogram indicated impaired renal function and the blood urea was 72 mg.%. Dental examination revealed a myeloid epulis in relation to the lower left second molar tooth.

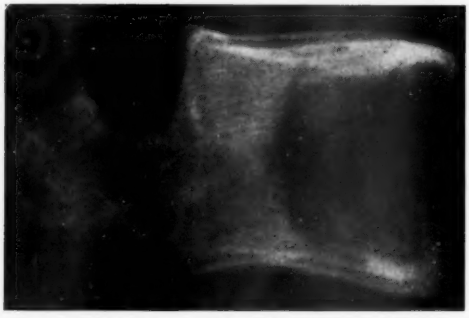

FIG. 1.—Second lumbar vertebra showing osteolytic change.

Operation.—A biopsy taken from the affected area of the left fibula on 21.4.52 confirmed the diagnosis of osteitis fibrosa cystica.

Exploration of the neck was undertaken by Mr. Dickson Wright on 5.5.52. An enlarged parathyroid gland about the size of a cherry was removed from the lateral aspect of the left lobe of the thyroid. The remaining parathyroid tissue appeared to be unaffected, and it is therefore of interest that, in the opinion of Professor W. D. Newcomb, the excised gland was hyperplastic rather than adenomatous.

Progress.—The post-operative course was uneventful and removal of the active tissue appears to have been complete. The serum calcium fell to 10 mg.% by the fifth post-operative day and has remained within normal limits. At the same time improved kidney function was shown by a reduction in the blood urea to 52 mg.%. The myeloid epulis disappeared without treatment, and all bone lesions are showing evidence of repair, although it is still necessary for the patient to wear a spinal brace.

Comment.—The vague bone pains, asthenia, and intestinal disturbances of early hyperparathyroidism form an ill-defined symptom-complex which is also seen in functional disease. It is therefore important to keep the possibility of hyperparathyroidism in mind when investigating such cases, if the disease is to be detected at the crucial stage before skeletal deformity or metastatic calcification has occurred.